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LIPOMA OF THE ORAL CAVITY

A. Bergenholtz, L.D.S., and H. Thilander, L.D.S.,** Umeå, Sweden*

THE word *lipoma* is derived from the Greek *lipos* (''fat'') and *oma* (''tumor''). It is the name of a slowly growing tumor that consists chiefly of fatty tissue, similar in structure to physiologic fatty tissue. A lipoma is largely lobated through septa consisting of connective tissue, each lobe corresponding to the expanded area for an artery.[6] Lipomas may attain considerable size.

A fibrolipoma is a type of lipoma which is more compact because of a greater interstratification of connective tissue. Fibrolipomas are considered to be the more common type. There are also other types of lipoma found in connection with nerve tissue (neurolipoma), mucoid tissue (myxolipoma), blood vessels (angiolipoma), etc.

A case of metastasizing lipoma, the so-called ''liposarcomatosis'' is occasionally described in the literature.[13, 18, 46] This type, however, is extremely rare and, strictly speaking, should not be considered a lipoma at all.

INCIDENCE

Lipomas are among the most common neoplasms. They often occur in the subcutaneous fatty tissue, particularly in the shoulders, back, neck, and throat.[18, 39] Other common locations are the mesentery and the retroperitoneal fatty tissue.[6] They occur less frequently in the subcutaneous region of the face, the scalp, and the more peripheral parts of the extremities. A relatively rare kind of diffuse lipoma is the so-called ''Madelung's neck.'' Lipomas in the mouth are exceptionally rare. In a series of 490 cases of lipoma, Geschickter[18] found only three with an oral localization. Amadeu Carvalho de Almeida,[1] in an investigation comprising 1,427 biopsies of the tongue, reported 846 tumors, only three of which were lipomas.

From the Department of Oral Surgery (Head: Prof. Dr. John Hertz, M.D.), The Royal School of Dentistry in Stockholm and Umeå.
*Oral Surgeon, Royal School of Dentistry, Umeå, Sweden.
**Associate Professor of Oral Surgery, Royal School of Dentistry, Umeå, Sweden.

Lipomas most frequently occur in patients between 30 and 50 years of age. This age group constituted 75 per cent of the series of 170 cases reported by Sommerville and Wakeley[39] and 55 per cent of Geschickter's[18] series of 490 cases. In 10 per cent of the latter series, lipomas were found in children under 10 years of age.

Concerning the distribution of lipomas according to sex, Gorsch,[20] in a study of 700 patients found a preponderance among the female patients (62 per cent of the tumors occurred in women and 38 per cent in men). Geschickter[18] obtained similar results (a ratio of three to two in 490 cases), as did Sommerville and Wakeley (a ratio of two to one in 170 cases). Hennigsen's[24] results were in quite the opposite direction, as 61 per cent of his patients were men and 39 per cent were women.

No increased frequency of lipomas in particularly corpulent persons has been observed. This, of course, is a remarkable feature as far as the etiology of lipomas is concerned. Moreover, starvation cures will not eliminate lipomas.

In the mouth, the most common area of predilection appears to be the tongue, particularly the tip, close to the midline and the lateral regions, submucously, interstitially, or intramuscularly.[12, 25] Lipomas are also found where fatty tissue normally occurs (for example, in the vicinity of Bichat's fatty body). Other areas of predilection are the cheeks, the gums, the floor of the mouth, and the lips. Lipomas very seldom occur in the gingiva.[30] In 1949, Quinn[36] reported a case of lipoma in the soft tissue corresponding to the foramen mentale, another extremely rare localization.

Lipomas are very infrequent in the bone tissue, particularly in the mandible and the maxilla. Dickson and associates[15] reported a case of true lipoma in the tibia, and Oringer[34] and Mead have described two cases of lipoma in the maxilla.

Lipomas often may occur in connection with endocrine disorders, the most important of these being adiposogenital dystrophy and adiposis dolorosa.

ETIOLOGY

The etiology of lipomas has never been satisfactorily determined. In the 1850's Virchow stated that lipomas were due to either a hereditary or an acquired disposition. Many modern authors also emphasize the significance of heredity.[39, 51] It has been suggested that nonretracted fatty tissue is a cause of lipoma. Trauma has also been mentioned as an etiological factor; later investigations, however, proved unable to confirm this assumption. Poncet[35] stressed the connection between tuberculosis and the formation of lipomas. He considered this quite natural in view of the fact that tuberculosis is of a hyperplastic nature, and he believed that consequently there is a possibility that lipomas may occur in tuberculous patients.

PATHOGENESIS

It used to be assumed that adipose tissue was simply connective tissue in which fat was stored. This conception, however, was modified by Toldt,[42] who

stated that adipose tissue was a special kind of tissue which originated in particular areas and organs; it was characterized as a highly vascular lobated tissue in which a special type of cells were stored and which served as a fat depot. In 1926 Wassermann[45] and his colleagues proved that adipose tissue had a certain relationship to the undifferentiated mesenchymal cells.

According to Wells,[47] the first studies on the formation of lipomas were carried out by Borst[7] in 1902, and Bender[4] in 1903. Borst and Bender found that lipomas originated from the preadipose tissue, which is similar to that of normal, mature fat.

As mentioned previously, some authors consider that the origin of lipomas is nonretracted, fetal fatty tissue. Such embryonic fatty tissue is found in the neck and shoulder areas in the embryo and has been named "interscapular glands" by Hatai.[22] Embryologists claim that these "interscapular glands" have a function as a lipoid "storehouse" corresponding to the hibernating glands of insects and animals. It is possible that this type of tissue can be found in the oral cavity of the embryo and that it does not retrogress after birth but remains dormant until it becomes active later in life, forming lipomas. The relationship between the so-called embryonic lipomas and the true lipomas has been described by van Meurs.[29]

The relationship of lipomas to the attendant fat in physiologic metabolism has long been the subject of interest, but up to now no solution of the problem has been reached.

Concerning the genesis of lipomas, Gorsch[20] was of the opinion that their localization was in inverse ratio to the number of sebaceous glands and sweat glands present in a region of the body; through hyposecretion, more fat would be produced. Gorsch ascribed multiple lipomas to a disorder in the cerebral sweat-gland center, giving rise to a trophoneurosis of the skin. The connection between peripheral nerves and lipomas has often been mentioned.

Sommerville and Wakeley[39] state emphatically that there are no grounds whatever for thinking that any connection exists between the formation of lipomas and the hormonal changes in the organism during puberty or menopause. Other investigators, however, have found a hormonal relationship between acne vulgaris, sebaceous glands, fat retention, and puberty. This problem calls for a great deal of further investigation.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

A lipoma is characterized clinically as a benign, slowly growing, soft, freely movable, usually lobated tumor. Sometimes the tumor may be pedunculated, but it is usually attached to a broad sessile base. If the tumor is located near a surface, it has the appearance of a yellowish, shimmering growth. On palpitation, the tumor feels spherical, often pseudofluctuating. A characteristic feature of surface lipomas is the visibility of the subepithelial blood vessels.[40]

A lipoma usually causes no discomfort to the patient, except when it becomes troublesome because of its size or when its position prevents physical

function. Thoma[40, 41] has described the case of a lipoma situated in the infratemporal fossa, which proved painful during mastication because of its pressure on the nerves. Such cases, however, are rare. Usually there is no discomfort unless mastication causes ulceration and subsequent infection.

Because of its consistency and form, a lipoma may be confused with a mucocele and sometimes with a ranula[14] or a dermoid cyst. According to the literature, deeper-lying types may also be mistaken for abscesses. Of course, such mistakes may occur where there are connective tissue tumors or different types of cysts.

For diagnostic purposes, von Mikulicz and Kümmel[30] have suggested diaphanoscopy, particularly in cases of lipoma in the mouth, as cysts appear translucent whereas lipomas appear dark.

X-ray examinations are not very helpful in the diagnosis of lipomas. Thoma suggests an x-ray examination in the form of a so-called "lamellogram," that is, a kind of planigraphy with either very soft rays or very hard rays.

After extirpation, a preliminary diagnosis can be made macroscopically by virtue of the structure of the fatty tissue, but the specimen should always be examined microscopically for verification.

Microscopic examination of the slow-growing lipoma reveals a tissue which differs very slightly from normal fatty tissue. In tumor tissue, however, there are cells rich in protoplasma and filled with small drops of fat, that is, lipoblasts.[6]

According to Thoma, the embryonic type of lipoma, with large fat cells, granular cytoplasm, and centrally situated nuclei, indicates a tumor of faster growth.

THERAPY

The treatment of a lipoma involves total surgical extirpation. Many consider this unnecessary, except for esthetic reasons, if the position of the tumor is not injurious to the patient. If extirpation is not total and remnants of the tumor tissue have been left behind, there is always the risk of recurrence. According to Weil,[46] a recurrence may give rise to malignancy; this, however, is a very rare complication.

The case reported by Weil concerns a 69-year-old man with a recurrent lipoma at the base of the penis. From 1940 to 1948 he was operated upon five times. The histologic features changed from true lipoma to fibrolipoma and so on to lipomyxofibroma with malignancy suspected and finally evident. A biopsy in 1951 led to the diagnosis of fibromyxoliposarcoma.

CASE REPORT

History and Examination.—A slim 49-year-old painter was admitted to the Department of Oral Surgery of the Umeå Royal Dental School because of a slow-growing swelling in the mouth in the region between the lower right central incisor and second premolar. He had noticed the swelling eight months previously. The tumor, thought to be a cyst, had

been punctured with negative results at a county dental policlinic. Occasionally, when touched or rubbed, the swelling increased, but after a while it resumed its previous size. There was no pain or any other discomfort.

Extraoral examination revealed a swelling outside the right mental foramen, which extended from the midline to the region of the lower right premolars. Intraoral examination revealed a nontender, cystlike, fluctuating swelling limited to the above-mentioned area. There were no signs of inflammation and no involvement of the lymph nodes. The remainder of the patient's bite consisted of $\lceil \overline{5}\text{———}\overline{4} \rceil$ and $\lfloor \overline{7}, \lfloor \overline{5}, \lfloor \overline{3}, \lfloor \overline{1}\text{———}\overline{5} \rfloor$, all of which responded positively to a vitality test carried out with ethyl chloride and warm stopping gutta-percha.

A routine examination was essentially negative.

The roentgenograms revealed no apical radiolucency or any other rarefied zones.

As a result of the clinical findings and the absence of inflammatory symptoms, the preliminary diagnosis was lipoma of the oral vestibule in the region of $\overline{1}\rfloor\text{———}\overline{5}\rfloor$.

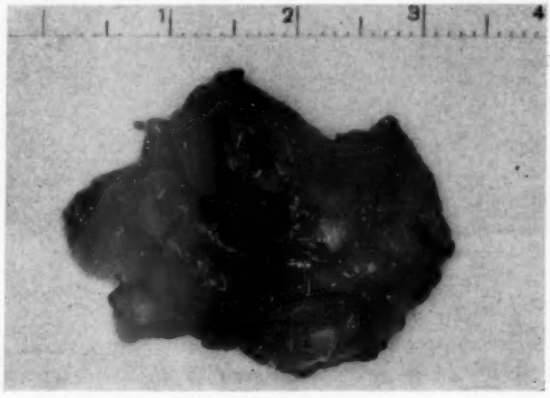

Fig. 1.

Treatment.—Surgery was performed following induction of local anesthesia, through an incision in the $\lceil \overline{1}\text{———}\overline{5} \rceil$ region about 1 cm. below and parallel to the gingival margin. An obtuse, yellowish, capsular tumor formation was isolated from the surrounding tissue by means of dissecting scissors and a periosteotome (Fig. 1). The mental nerve was in the immediate proximity of the base of the lipoma, and several fine branches were seen to spread to the tumor. For this reason, isolation was performed with very great care. The wound was sutured without drainage.

Pathology.—The removed tissue consisted of partly lobated fat. It had a slight tendency toward marginal demarcation with no proper encapsulation. The fat was supported by a scanty stroma containing blood vessels. Areas of highly differentiated skeletal musculature were observed, partly as a marginal capsular formation and partly interwoven in the fatty tissue, accompanied by blood vessels and nerves. Nothing suggested that the skeletal musculature really constituted a neoplastic component, although anatomically it was so closely bound up with the fat that it may be assumed that the lipoma formation originated from interstitial muscle tissue. The fatty tissue assumed a partly embryonic structure, particularly in the muscular relationship. There was no evidence of malignancy. *Diagnosis (Dr. B. Larsson):* Lipoma, probably originating from a muscle interstice (Fig. 2).

Postoperative Course.—The postoperative course was uneventful, aside from an insignificant postoperative edema which was observed the following day but disappeared a

few days later. There was no paresthesia in the region of the mental nerve. When the patient left the hospital five days after the operation, there was only a slight discoloration in the right mental region.

Final Outcome.—Follow-up examination ten months after surgery revealed good healing, and there was no clinical evidence of recurrence.

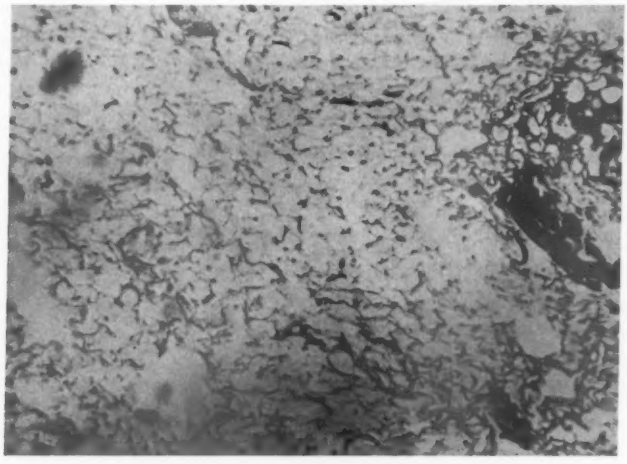

Fig. 2.

COMMENTS

The foregoing case of a true lipoma in a 49-year-old man may be considered unique. As a survey of the literature shows, it is extremely rare for this kind of tumor to be located in the oral region, especially in the soft tissue immediately outside the mental foramen.

Generally speaking, we rarely have to deal with true lipomas. Usually, we are confronted by the much more common variants, such as fibrolipomas.

It is interesting to note that in certain areas lipoma tissues have a typical embryonic character. Embryonic remnants may have been latent in the region and may have become proliferative as a result of some unknown irritant.

The pathogenetic factors in this lipoma are very difficult to establish. Nevertheless, certain interesting features may be mentioned. Microscopic examination revealed an intimate relationship between the fatty tissue and the muscle interstices in those areas of the skeletal musculature which occur as a result of tumor formation. This may indicate that the lipoma developed from a muscle interstice.

Further, emphasis must be placed upon the intimate relationship between the lipoma and the mental nerve and its branches. The relationship of the nerves to the lipoma is often stressed in the literature. The absence of pain despite the intimate relationship with the mental nerve may be explained by the compliance of the surrounding soft tissues, which caused no increased pressure on the nerve.

SUMMARY

Lipomas are defined, and their occurrence, etiology, pathogenesis, clinical features, differential diagnosis, and treatment are discussed, with references to previous literature.

A case of lipoma of the oral labial vestibule is reported, and the etiology and pathogenesis are discussed. We consider that the lipoma described was of embryonic origin.

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ROYAL DENTAL SCHOOL
UMEÅ 2, SWEDEN

CERVICOFACIAL ACTINOMYCOSIS OF THE MANDIBLE

Marvin E. Pizer, D.D.S., M.S., Alexandria, Va.

ACTINOMYCOSIS is an infectious, inflammatory disease which may be either subacute or chronic. The cervicofacial variety is the most common form of this disease; in more than one-half of the cases seen the cervicofacial region is involved, rather than the thoracic and gastrointestinal regions.

The disease usually spreads by tissue expansion, although primary cutaneous lesions have been known to metastasize to visceral organs, including the lungs.

The characteristic clinical picture of cervicofacial actinomycosis frequently follows the extraction of teeth. Swelling, trismus, and nodules on the gingiva are the initial findings. These nodules enlarge slowly, until eventually they break down and discharge a yellowish fluid which generally contains "sulfur granules."[1] More nodules continue to appear, with a resulting boardlike swelling of the submaxillary and cervical regions. These submandibular swellings break down, and the resulting cutaneous fistulas then discharge the "sulfur granules" which represent colonies of *Actinomyces bovis.*

The *Actinomyces bovis,* a frequent inhabitant of the mouth, is thought to be the etiological agent of this disease. In addition to the oral cavity, the actinomycetes are also seen in the soil and on grasses. The organism is basically parasitic.

Such diseases as syphilis, alveolar abscess, tuberculosis, blastomycosis, and histoplasmosis should be considered in the differential diagnosis. Direct smears, biopsy, and culture studies are necessary for establishing the diagnosis.[2]

Various forms of therapy have been employed in the treatment of actinomycosis. These include surgery, irradiation, and the use of vaccines, sulfonamides, and broad-spectrum antibiotics, as well as potassium iodide, methylene blue, and copper sulfate.[3]

CASE REPORT

A 35-year-old white man was first seen in the office on Oct. 1, 1956. His chief complaint was of periodic pain in the right mandible with intermittent episodes of discharge both intra- and extraorally.

The past history given by the patient revealed that the pain began spontaneously in the anterior portion of the right mandible. The patient consulted his physician, who administered antibiotics but to no avail. A second physician could find no pathology and referred the patient to a dentist, who extracted some anterior teeth in the mandible. Following these extractions, which were performed approximately one month after the

original symptoms appeared, swelling began in the submental region of the right mandible. The cause of this swelling could not be ascertained, and the patient's dentist referred him to another physician. This physician examined the patient and took roentgenograms but could not find the cause of the submental pathology. Another submandibular swelling began, and the patient consulted another physician, who treated the swelling by incision. The patient was referred to an otolaryngologist, who took additional roentgenograms and incised additional submandibular swellings. The patient was next advised to return to his private dentist, who in turn removed all the mandibular teeth except the left first, second and third molars. The patient's symptoms persisted, however, and an oral surgeon advised him to leave the situation alone as it was "only a skin infection." This was approximately one year after the original symptoms had appeared. For the next year, the patient had intermittent drainage from the cutaneous fistulas in the right submaxillary and submental regions and the buccal sulcus of the mouth. The remaining past medical and surgical history was noncontributory. A history of penicillin sensitivity was elicited at this time.

Fig. 1.

Fig. 2.

Fig. 1.—Preoperative view showing "lumpy" appearance of jaw. This swelling is extremely indurated.

Fig. 2.—Old incisions and multiple fistulas are visible in this preoperative view of the submental region.

A smear taken from a draining submental fistula on Oct. 1, 1956, revealed typical colonies consistent with *Actinomyces bovis*. A complete blood count revealed 6 per cent eosinphils.

The patient was admitted to the Alexandria Hospital on Oct. 12, 1956. A complete history was taken. The general physical examination and routine blood and urine studies

were within normal limits, except for an elevated eosinophil count. A chest film revealed no additional findings. On intraoral examination, the clinical appearance of the hard and soft tissues of the mouth was normal except for a draining fistula in the buccal vestibule in the region of the mandibular right first molar. Extraorally, there were multiple cutaneous fistulas in the submental and submaxillary regions of the right side. Much of the swelling in the right submaxillary and submental regions was indurated, especially below the inferior border of the mandibular first molar. Old scars where previous attempts at incision and drainage had been made were detectable (Figs. 1 and 2).

Roentgenograms of the right mandible revealed several vertical radiolucent areas extending from the alveolar process downward toward the inferior border in the region of the first molar. These probably represented fistulous tracts. Some could be traced with Lipiodol injected through a needle (Fig. 3).

Initial orders, in addition to routine laboratory studies, included potassium iodide, 5 drops three times a day; Abdec vitamin capsules; and erythromycin, 250 mg. tablet every four hours. On October 13, the potassium iodide dose was increased to 15 drops three times a day, and on October 14 it was raised to 25 drops three times a day. (Incidentally, the eosinophil count dropped to normal twenty-four hours after this therapy was initiated.) The dose of potassium iodide was increased to 30 drops three times a day on October 15. From October 12 to October 16 there was considerable improvement, both subjectively and objectively. A significant degree of the submental induration had subsided.

Fig. 3.—Lateral view of right mandible taken before surgery. Note radiopaque dye being injected into the fistula.

The patient was taken to the operating room on Oct. 17, 1956. After general endotracheal anesthesia had been induced, a skin incision was made about 1 cm. below the inferior border of the mandible, beginning 2 cm. anterior to the angle of the jaw and extending to the symphysis of the right side. The mandible was exposed by sharp and blunt dissection and was found to be eroded at the inferior border near the symphysis. The area was curetted until healthy bone was approached. The cutaneous fistulas were either excised or cauterized with phenol. The soft tissues were of leather-like consistency, and only minimal tissue vascularity was visualized. The wound was closed in layers, with 000 chromic sutures for the deeper tissues and 00000 silk sutures for the skin. Two drains were inserted—one near the symphysis and the other near the angle of the jaw. The second part of the operation included intraoral surgery. A mucoperiosteal flap was reflected from

the ramus of the right mandible to the mental foramen. The tract of the fistula was curetted and cauterized with phenol. All fistulas cauterized with phenol were neutralized with alcohol. The mucoperiosteal flap was next placed back into position and sutured with 000 chromic interrupted sutures. The patient left the operating room in good condition.

Postoperative medication consisted of erythromycin, 250 mg. every four hours, and 30 drops of potassium iodide three times a day. The other postoperative orders were routine.

Fig. 4. Fig. 5.

Figs. 4 and 5.—Six months after surgery.

Fig. 6.—Intraoral healing is evident. Closure by primary healing.

The drain in the submental region was removed on the first postoperative day. There was extensive drainage from the submental area. On the second postoperative day the submaxillary drain was removed, although there was still copious drainage. On Oct. 20, 1956, the third postoperative day, drainage from the neck began to decrease. Alternate oral and skin sutures were removed on Oct. 21, 1956. Extraoral drainage still persisted; the dressing was changed daily. On Oct. 22, 1956, the remainder of the sutures were removed. The patient's condition was much improved on Oct. 24; extraoral drainage had all but ceased, and the submaxillary and submental induration and swelling were remarkably reduced. The patient was discharged from the hospital on Oct. 25, 1956. He was given a prescription for erythromycin tablets which were to be taken for the next week.

When the patient was seen at the office on Nov. 1, 1956, the neck incision had closed completely. There was no drainage. Intraorally, the wound had closed by primary intention, and there was no evidence of any fistulous tract.

The patient was seen on Dec. 31, 1956, and again on April 15, 1957. His condition had improved dramatically. The "lumpy" appearance of the submaxillary and submental soft tissues on the right side had decreased remarkably (Figs. 4 and 5). The overlying skin in this region was freely movable, and the minimal induration represented only the scar tissue. Intraorally, there was no evidence of disease (Fig. 6). The patient had been completely asymptomatic. Photographs taken more than one year after treatment revealed complete healing (Figs. 7 and 8).

Fig. 7.

Fig. 8.

Fig. 7.—Anteroposterior photograph showing marked cosmetic improvement and no evidence of active disease one year after surgery.
Fig. 8.—Lateral view of submental and submaxillary regions one year after treatment.

DISCUSSION AND CONCLUSIONS

The findings in the foregoing case are characteristic of cervicofacial actinomycosis: the multiple draining fistulas from the skin of the submandibular region, the boardlike consistency of the submandibular nodes, the purplish color around the discharging fistulas, the patient's history of dental extractions prior to oral manifestations, the elevated blood eosinophil count (found in parasitic disease), and the direct smear producing a culture that contained characteristic colonies of *Actinomyces bovis.*

Immediate treatment consisted of heavy doses of an antibiotic and increasing doses of potassium iodide. Penicillin would have been the antibiotic of choice, but since the patient presented a history of sensitivity to this drug it was necessary to use another antibiotic, namely, erythromycin. When it was felt that the blood level of the antibiotic was at its peak and the limit of tolerance to potassium iodide had been reached, surgical intervention was next employed. After the operation the patient received the same antibiotic and potassium iodide that he had been given preoperatively. In all, only three weeks of intensive antibiotic therapy were needed. There was copious postoperative drainage until the potassium iodide was discontinued; then healing occurred without complication. There was a remarkable reduction of the induration in the submandibular region.

It was not possible to trace the fistulas in the mandible completely. Some of the cutaneous fistulas could be traced to the inferior border of the jaw.

I feel that this patient has been cured by a combination of intensive antibiotic therapy, potassium iodide, and surgical intervention. In addition, this therapy has produced a cosmetic improvement. I also feel that the combination of surgery, potassium iodide, and antibiotic therapy can produce a cure more rapidly than the administration of antibiotics alone over a long period of time. Antibiotics are generally incapable of penetrating all the crypts and tracts that are surrounded by granulation tissue; therefore, they cannot attack all the organisms.

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AMELOBLASTOMA DEVELOPING FROM A DENTIGEROUS CYST

Rafael Madan, D.D.S., Havana, Cuba

AMELOBLASTOMAS are tumors of epithelial origin that appear with great frequency in the maxilla and mandible.

They may be derived, according to Thoma,[1] from (1) genetic disturbance of the enamel organ or the tissue forming it; (2) cell rests of the enamel organ, either during tooth development or later; (3) the epithelium of odontogenic cysts; (4) the surface epithelium covering the jaw; and (5) displaced epithelium in other parts of the body.

The relatively small number of cases in the literature which show that ameloblastomas can develop from odontogenic cysts has influenced me to publish the following case.

CASE REPORT

A. G. S., a 15-year-old Negro boy, was admitted to the Curie Hospital because of a tumor of the face.

A year before, he had received a blow to the face, and a month afterward the mandible started to swell until it reached the present size.

Clinical Examination.—The patient, a rather thin, undernourished boy, presented a swelling of the left side of the face (Fig. 1). The intraoral examination revealed a smooth, bulging tumor, without any change in color of the mucosa. It had the consistency of a rubber ball, and it extended from the left lower first molar to the ascending ramus on the same side (Fig. 2).

X-ray Examination.—The anteroposterior and lateral jaw films showed a large osteolytic lesion on the left side of the mandible, producing a thinning of the cortex. At the inferior border the lower first molar could be seen, but there was no evidence of the second or third molars having formed (Figs. 3 and 4).

Laboratory Findings.—Blood studies revealed the following: R. B. C., 4,400,000; leukocytes, 8,000; hemoglobin, 84; eosinophils, 0.1; neutrophils, 69; lymphocytes, 28; monocytes, 0.2. Bleeding and coagulation times were within normal limits; the serology was negative, and the blood chemistry findings were essentially normal.

In view of the above-mentioned findings, our impression was that we had to deal with an ameloblastoma developing from a dentigerous cyst as a consequence of the blow that the patient had received a year earlier.

Operation.—Under intravenous Pentothal sodium anesthesia, with gas and oxygen administered through a nasal endotracheal tube, a curved incision was made in the neck 1 cm. below the inferior border of the mandible, extending from the mastoid process to the midline. After careful dissection to avoid cutting the mandibular branch of the facial

nerve, the mandible was exposed. It was found to be deformed and enlarged. The periosteum was carefully stripped from the bone, after which the mandible was cut with a Stryker saw 1 cm. away from the tumor anteriorly. Then, by blunt dissection, the mandible was further exposed by detaching the masseter and internal pterygoid muscles. The condyle had a dark bluish color, so it was decided to include it in the resection. The left side of the mandible was thus removed "en bloc" (Fig. 5). A hemorrage started from the glenoid fossae and could not be controlled in the usual way. Gelfoam soaked in

Fig. 1.—Bulging of the tumor producing a marked deformity of the face.

Fig. 2.—Intraoral view showing the complete obliteration of the buccal sulcus.

thrombin was packed into the wound, and a strip of iodoform gauze was inserted to apply pressure. The wound was closed in planes with catgut 000, and silk was used to close the skin. Ample space was left open so the iodoform gauze could be removed easily later.

The recovery was uneventful. The iodoform gauze was removed on the second postoperative day. The patient was kept on a combination of streptomycin and penicillin

(1 Gm. per day for ten days). The skin sutures were removed on the sixth postoperative day.

Histopathology.—The pathology report from Dr. Masó* was as follows: "the specimen consists of a cystic tumor of the mandible, 12 × 5 × 3 cm. in size. The walls are thin, 2 to 6 mm. in width. In the inside the crown of a molar tooth was found. The internal wall presented little masses of proliferating tissue."

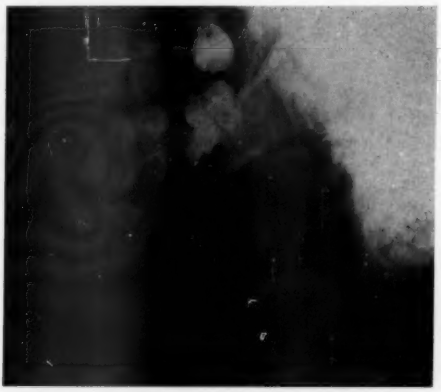

Fig. 3.

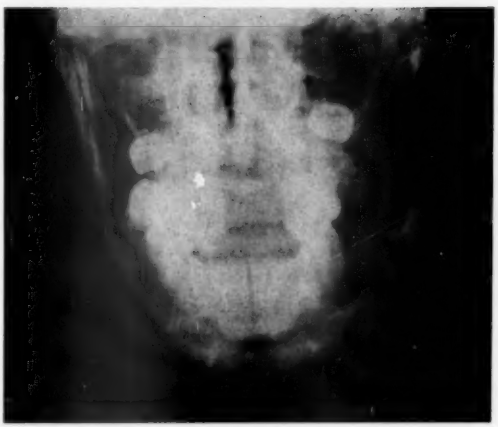

Fig. 4.

Figs. 3 and 4.—Lateral and anteroposterior views showing the "cystic" lesion, with a molar displaced at the inferior border of the mandible.

In the microscopic section, solid cords of epithelial cells surrounding a stellate reticulum resembling the enamel organ were found. The stroma was composed of a loose connective tissue.

Diagnosis: Ameloblastoma arising from the wall of an odontogenic cyst.

*Dr. Calixto Masó, Sub-director of the Institute de Cito-Diagnostico, Hospital Curie, Havana, Cuba.

DISCUSSION

It should always be remembered that dentigerous cysts may develop into ameloblastomas, and since Cahn[2] has sounded the alarm with his article entitled "The Dentigerous Cyst as a Potential Adamantinoma," a large number of the so-called "cysts," on histologic examination, have been found to be ameloblastomas.

With this in mind, partial operations may be of great danger. If some of the membrane of a so-called "cyst" is left behind, this may be part of an ameloblastoma or it may develop into one. The treatment should always consist of complete enucleation of the so-called "cystic membrane," and in every case a histologic examination should be made.

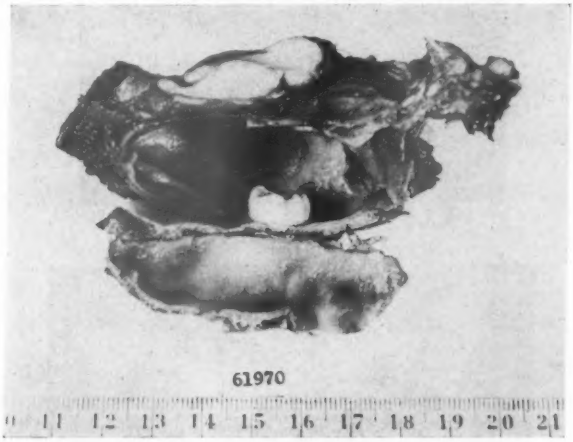

Fig. 5.—The specimen opened, showing the cystic tumor with its thin walls and the molar tooth.

Bernier[4] has published the following statistics which show the very close relationship between cysts and ameloblastomas:

Ameloblastomas Associated With Cysts

	Number	*Per cent*
Association	29	33
No association	20	23
Undetermined	39	44
Total	88	100

Although ameloblastomas are considered benign tumors, they sometimes do not act like benign tumors. This should always be taken into consideration in their treatment. They occasionally can cause death, either by local invasion or by metastases, as has been reported by Sharp and associates.[3]

Therefore, the treatment should be radical. No curettage is safe; complete excision of the tumor with a safe margin of healthy tissue is the best

Fig. 6.

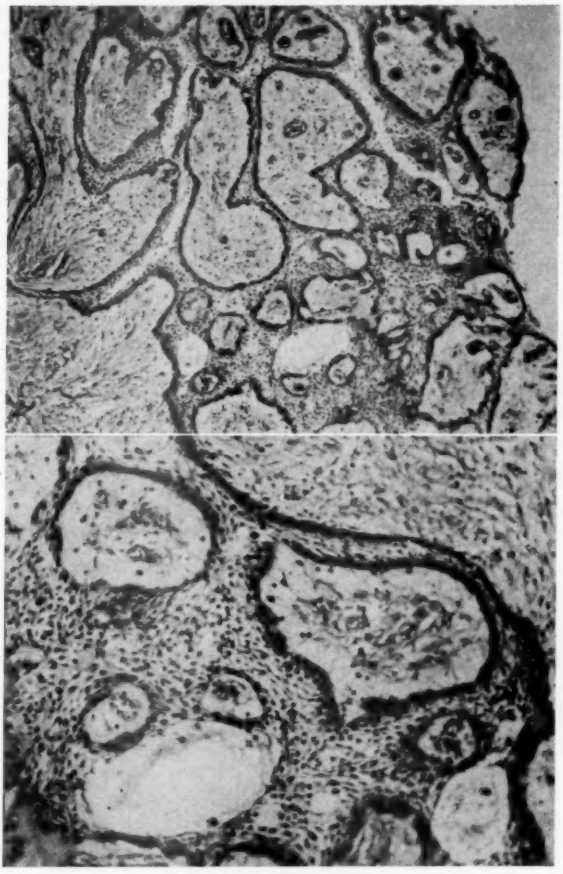

Fig. 7.

Fig. 6.—Solid strands and cords of epithelial cells with a loose stroma.
Fig. 7.—At higher magnification, the epithelial cells adopt the typical palisade form.

procedure. Bernier,[4] in his book entitled *Management of Oral Disease,* published the following statistics:

Type of Treatment and Recurrence

Type of Treatment	*Total*	*No Recurrence*	*Recurrence*	*Not Informed*
Conservative	70	25	20	25
Radical	12	8	1	3
Undetermined	6	-	1	5
Total	88	33	22	33

On the basis of the clinical examination and roentgenographic studies, five possible surgical procedures are proposed by Sharp and associates:[5]

1. Partial resection of the alveolar ridge for the early superficial lesion occurring in the alveolar crest where the roentgenographic evidence of invasion is confined to alveolar bone. A block specimen should be removed with at least a 1 cm. margin of normal bone on all sides.

2. Intraoral hemiresection is indicated in the mandible for larger lesions which are still confined within the bone and in the maxilla when the disease is confined to the lower half.

3. External partial resection of the mandible with immediate bone graft is indicated for more extensive tumors where it is possible to adapt an immediate graft for maintenance of normal alignment of the dental arches. Metal or plastic splints may be more appropriate in certain cases.

4. External hemiresection of the mandible with a radical neck dissection is indicated only for the carcinomatous type of growth involving the mandible.

5. Total resection of the maxilla, often with the contents of the orbit, is indicated for the majority of the extensive maxillary ameloblastomas and for all ameloblastomas with carcinomatous changes. An accompanying radical neck dissection is indicated only if cervical nodes are clinically demonstrated to be involved.

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PARTIAL ANKYLOGLOSSIA

Report of a Case

Richard Spitzer, D.M.D., London, England

ANKYLOGLOSSIA is a congenital developmental condition, generally referred to as tongue-tie, in which there is an abnormal fixation of the tongue to the floor of the mouth and/or to the lingual aspect of the gingival mucosa due to a short and malpositioned frenulum linguae.[6, 8] When this anomaly is present, nursing and feeding difficulties often arise soon after birth, necessitating the sectioning of the fibrous band. Consequently, ankyloglossia is rarely found in infants,[2] and it is even less common in adult patients. Therefore, a brief report of a case of ankyloglossia may be of interest.

Fig. 1.—Curling of the tongue and downward arching of its tip on attempted protrusion due to its abnormal attachment.

CASE REPORT

Mrs. N. T., aged 49 years, was referred from the Geriatric Outpatients Department. The patient had difficulty with mastication and complained of a painful sensation in both temporomandibular joints. Her main complaint, however, had to do with the hypomobility of her tongue which had interfered with normal chewing and swallowing all her

From the Dental Department, St. John's Hospital, London, S.W. 11, England.

life. The condition had also given rise to imperfect speech and a marked lisp, features of which she was painfully aware. Surgical correction of the anomaly had never been suggested to the patient.

Examination disclosed a notable overclosure and malocclusion. The patient was wearing partial dentures. Tongue mobility was grossly limited by a thick and short frenulum which was broadly fused to the ventral surface of the tip of the tongue and to the lingual aspect of the gingiva. Any modification of the shape of the tongue essential for both chewing and swallowing was difficult to achieve (Figs. 1, 2, and 3).

Fig. 2.

Fig. 3.

Fig. 2.—Restricted movement in the vertical plane due to anteriorly shifted frenulum linguae.

Fig. 3.—Horizontal protrusion grossly restricted.

The patient was operated on under bilateral block anesthesia for the primary purpose of freeing the tongue of its abnormal attachments. As a result of the operation, the patient was soon able to masticate properly. Impressive also was the beneficial effect on the patient's psychological disposition when the disorders of speech and deglutition had been corrected (Figs. 4, 5, and 6). The symptoms of a temporomandibular joint disturbance were readily corrected by the insertion of a bite plate.

I am indebted to Dr. T. H. Howell, F.R.C.P., for referring this case to me.

Fig. 4.

Fig. 5.

Fig. 6.

Figs. 4 to 6.—Postoperative results.
Fig. 4.—Normal excursion of the tongue.
Fig. 5.—Normal movement in the vertical plane.
Fig. 6.—Normal excursion in the horizontal plane.

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EXODONTIA

HEMATOMA FOLLOWING DENTAL EXTRACTIONS IN A PATIENT RECEIVING UNREPORTED ANTICOAGULANT THERAPY

Jack Schmitt, D.D.S., R. C. Ingram, D.D.S.,** and H. James Harpole, D.D.S.,*** Atlanta, Ga.*

INTRODUCTION

ANTICOAGULANT therapy with heparin and Dicumarol is effective in diseases in which intravascular clotting is to be avoided. There is also evidence that these agents may be effective in the dissolution of early thrombus material. In the practice of medicine today, patients afflicted with venous thrombosis, intracardiac thrombi, pulmonary embolism, myocardial infarction, and acute arterial embolism of the extremities are often given anticoagulant therapy. Oral surgical procedures in patients known to be taking anticoagulants are extremely difficult. When the same procedures are performed upon patients whose anticoagulant therapy has not been reported to the oral surgeon, the postoperative complications are often difficult to manage, and if they are not handled properly death may result.[1]

CASE REPORT

A 66-year-old white man was admitted to the Veterans Administration Hospital in Atlanta, Georgia. His chief complaint was of weight loss and vomiting associated with the digestive cycle. He gave a history of having been treated for this complaint during the preceding four years. The only other significant feature of his medical history was treatment for cardiovascular disease in 1954, at which time he believed that he had received Dicumarol therapy. This therapy had been discontinued approximately one year later.

Two days after his admission, the Dental Service was asked to evaluate the patient for total dental extraction and construction of full dentures with a view to improving his eating habits. The Medical Service hoped that the digestive difficulties might be significantly reduced when the masticating function was improved.

*Senior Resident in Oral Surgery, Veterans Administration Hospital. (Mailing address: 1924 Hayes St., Nashville, Tennessee.)

**Chief of Dental Service, Veterans Administration Hospital, and faculty member, Emory University School of Dentistry.

***Chief of Oral Surgery, Emory University College of Dentistry and the Grady Memorial Hospital; Consultant in Oral Surgery to the Veterans Administration Hospital.

The patient was seen by the oral surgery resident, whose examination revealed that the dentition consisted of the mandibular cuspids and the lateral and central incisors. These teeth were mobile and involved with deep periodontal pocket formation. It was recommended to the Medical Service that the patient's remaining teeth be extracted and that complete dentures be constructed.

At the time of consultation, the blood count, urinalysis, VDRL, bleeding time, clotting time, and prothrombin time were within normal limits. The preliminary physical examination was negative. In view of these findings, the patient was scheduled for dental surgery. Two days later the patient was given premedication consisting of 100 mg. of Seconal sodium and 50 mg. of Demerol by mouth at 6:30 A.M. He was taken to the oral surgery room, where his mouth was cleansed with clear tincture of Merthiolate. He was then draped in the prescribed manner. Local anesthesia was induced with 2 per cent Xylocaine by bilateral mandibular blocks. The remaining six teeth were removed with forceps. The mucoperiosteum was elevated, and the underlying alveolar bone was trimmed and filed. The flap and periosteum were then repositioned and sutured with 0000 silk to allow primary healing. At the conclusion of the procedure hemostasis appeared adequate, and the patient was returned to his ward in good condition. Postoperative orders were written as follows:

1. Cold packs to mandible at twenty-minute intervals.
2. Liquid diet with in-between feedings as needed.
3. Multivitamin capsules twice a day.
4. Darvon, 32 mg. as needed for pain.
5. Check patient periodically for excessive bleeding.

Three hours after the procedure was completed the ward physician called to report that the patient had been started on heparin and Dicumarol therapy on the previous day, and he wanted to know whether any precaution should be taken to prevent excessive bleeding. The patient was seen immediately on his ward, where he seemed to be resting quietly. Intraoral examination revealed no abnormal bleeding. Several small areas of ecchymosis were visible in the symphysis area of the mandible.

At the conclusion of this examination the medical resident informed the oral surgery resident of the sequence of events that had led to the institution of anticoagulant therapy in this patient. On the day of the original dental consultation the Radiology Department had diagnosed a greatly enlarged heart during a fluoroscopic examination. In view of this finding, plus the past history of cardiovascular disease, it was decided that the patient should be given an anticoagulant to decrease the possibility of an intravascular thrombosis. Additional laboratory work had been ordered in conjunction with this therapy; however, this had not been noted on the patient's chart at the time of the surgical procedure. In addition, the Oral Surgery Division was not informed of this change in the therapy. A change of this type in a patient's therapy is always reported to the Oral Surgery Division. Due to the early operating schedule, however, the report was not received prior to the oral surgical procedure.

Because of this new development, the advisability of administering intravenous vitamin K was taken under consideration. In view of the lack of abnormal bleeding, however, the Medical Department stated that they preferred not to decrease the patient's prothrombin time because of the possibility of embolus formation.

It was decided that the patient should be observed and the previous orders continued. The first night was uneventful, and the following morning the patient appeared to be in good spirits in spite of a large hematoma over the symphysis area of the mandible (Fig. 1). Intraoral examination revealed no abnormal bleeding, and the suture line appeared normal. Cold compresses were continued, and hourly observation was ordered. The patient was informed of what had occurred, and his only comment was that he was glad that he had been in the hospital. The following three days were uneventful, and the patient progressed very satisfactorily. On the fourth postoperative day the ecchymotic area began to resolve (Fig. 2).

At this time the cold compresses were discontinued and hot moist packs were ordered in conjunction with warm saline mouth rinses every hour. On the seventh postoperative day the sutures were carefully removed without difficulty. At this time the discolored area over the symphysis was greatly reduced in size and was practically invisible (Fig. 3). By the fourteenth postoperative day the ecchymosis had completely resolved, and at this time the patient was referred to the Prosthetic Division (Fig. 4).

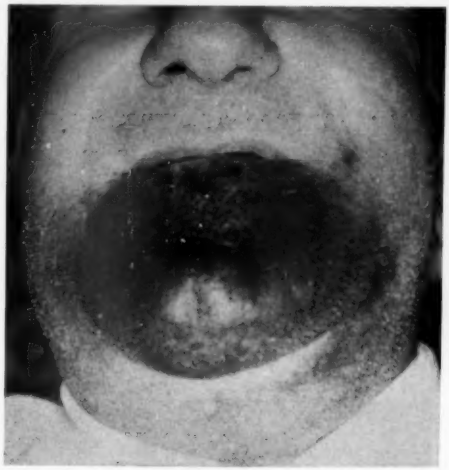

Fig. 1.—The patient one day after surgery. Note the large ecchymotic area over the symphysis.

Fig. 2.—The patient four days after surgery, showing partial resolution of the area.

SUMMARY

A case in which dental extractions were performed in a patient whose anticoagulant therapy was not reported to the oral surgeon has been presented. At

the time of surgery the patient's prothrombin time was 39 seconds, which was approximately 40 per cent. This case illustrates the close cooperation neces-

Fig. 3.—The patient on the seventh postoperative day.

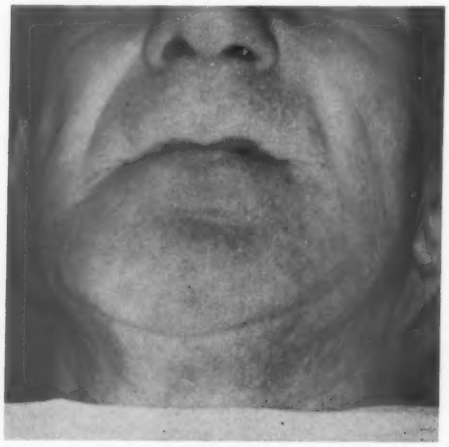

Fig. 4.—The patient fourteen days after surgery, at the time of his referral to the Prosthetics Division.

sary between the various services of hospitals in which patients are given complete medical care. It also shows the importance of obtaining a thorough history from outpatients for whom surgical procedures are contemplated.

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ORAL MEDICINE

ORAL CHANGE IN STURGE-WEBER'S DISEASE

I. Gyarmati, M.D., Gyula, Hungary*

STURGE described a disease in which he found congenital glaucoma, a circumscribed red spot on the face, nevus vasculosus, and epileptic convulsions contralateral to the nevus. This latter symptom, which he held to be secondary, allowed him to draw the conclusion that a vascular tissue proliferation similar to that on the face might exist in the cranium. Autopsy studies performed at a later date called attention to the fact that in addition to the glaucoma and the nevus vasculosus, which was located in the region of the trigeminal nerve, these cases presented also meningeal angiomatosis and cerebrocortical atrophy as well as calcification. The first roentgenologic presentation of this calcification is associated with the name of Parkes Weber. Bergstrand and associates,[1] therefore, apply the name Sturge-Weber's syndrome to the characteristic group of symptoms occurring on the head and caused by different vascular tissue proliferations. Hebold and several other authors in the recent literature consider the developmental disorders of the cranial vessels, principally the vessels of the skin and of the pia mater, to be significant in Sturge-Weber's disease, that is, in the disease caused by vascular tissue proliferations in the head. On the basis of this statement, Sturge-Weber's disease is, in fact, a developmental disorder which primarily affects the small vessels of the brain, the eyes, and the skin. Its further characteristic feature is that the abnormal blood vessels of the brain are prone to calcification, thus giving rise to typical x-ray changes. Not infrequently, the abnormalities manifest themselves in the form of tumors, but at any rate they may be traced back to the developmental disorders of the blood vessels. For several reasons, it is also obvious that a combined derangement of the nervous and vascular systems occurs in these cases. The best proof of this is the extension of the nevus vasculosus to certain nerve regions, most commonly to the area of the trigeminal nerve which, as is well known, supplies the teeth and the surrounding soft tissues with sensory nerves.

From the Stomatological Department, Békés County Hospital, Árpád-utca 24, Gyula, Hungary (A. Juba director).

*Head physician.

The anatomic changes very probably exist at birth, though later they may increase in extent. The embryologic development of the vascular system is a complicated process. The major part of the blood vessels does not come into being immediately but arises from the capillary network which partly undergoes regression and partly continues its development to give finally rise to the single vascular stems. Where the development of the vessels is more complicated, as in the head, it may well be that abnormal blood vessel formations develop. The way in which the arteries and veins differentiate has not yet been elucidated. Originally, the blood vessel formations showed complete bilateral symmetry. Only the retrogression, regeneration, and weaker and stronger development of certain parts give rise to the later asymmetries. It still is not known what factors cause these asymmetries. The mechanical moments of circulation probably have an important role, but they are able to provide a satisfactory explanation only if related to certain single cases. The case to be described here illustrates still greater importance of the fact that degenerations, transformations, and regenerations play a strikingly greater role in the final formation of the venous system than in the formation of the arterial system.

The cases described in the literature show that in Sturge-Weber's disease there may be an extreme variety of details, no matter what the main features may be. Olivecrona is of the view that a great many varieties and characteristic abortive cases exist with the classic triad of symptoms—glaucoma, facial nevus, and the calcifying cerebral process—which may show the greatest scale in ratio and manifestation. In the literature available to me, I could find among the diseases caused by vascular tissue proliferation of the head no data on developmental anomalies of the oral mucosa and, more precisely, of the gingivae. Therefore, the following case should be of interest.

Bergstrand differentiates three types of Sturge-Weber's disease: (1) the more severe cases, with epilepsy and idiotism, in addition to the entire triad of symptoms; (2) the less severe cases which present in general only two symptoms, but in which intracranial angiomatosis, if present, is associated with epilepsy; (3) the third group contains those abortive cases in which the nevus and the ocular symptoms are absent and in which merely the cerebral process with induced epileptiform symptoms is the most characteristic feature.

CASE REPORT

A 10-year-old girl was admitted in 1950 to the department of neurology and mental diseases of our hospital. She had a nevus flammeus on her face which had been present since her birth, and she had been having epileptic seizures almost daily since infancy.

State on Admission.—In addition to the facial nevus, there was a slight swelling of the upper lip and the upper gingiva, as shown in Fig. 1. On the basis of neurological examinations by Dr. A. Juba and repeated roentgenograms by Dr. Gy. Zétény, Sturge-Weber's disease was diagnosed (Fig. 2). Since the epilepsy failed to improve with treatment, and since the cerebral change had not proved to be extensive, the patient was operated upon in the autumn of 1953 at the Second Surgical Clinic by Prof. Imre Láng of the University Medical School in Szeged.

Operation: This consisted of a right temporo-occipital trepanation and partial extirpation of the occipital lobe. The epileptic seizures ceased after the operation. A striking increase, however, of the swelling on the upper gingiva was observed during the immediate postoperative weeks while the patient was still staying at the Surgical Clinic. These observations were reported also in the discharge notes of the Clinic.

Fig. 1.—Patient in first stage of disease. Note nevus flammeus on both sides of the face.

Fig. 2.—Roentgenogram of skull showing characteristic calcifications.

From this time on I had the opportunity to follow the oral manifestation and to photograph the progressive development (Figs. 3, 4, and 5) that took place until the patient's death in October, 1958.

According to the classification of Bergstrand, this case at the time of operation was classified as belonging to group 2, with intracranial angiomatosis and

secondary epilepsy, as well as nevus flammeus involving both the right and the left sides of the face. The swelling of the gingiva, however, which began to increase vigorously after the operation suggested that the abnormal vascular network caused by the irregular vascular development might have already infiltrated the corresponding area but that the infiltration had been in a state of rest until the surgical extirpation of the vascular proliferation. Then it turned into a rapidly increasing vascular tissue proliferation postoperatively, as shown in the photographs (Fig. 3).

Fig. 3.

Fig. 4.

Fig. 3.—Oral tumor caused by postoperative pathologic vascular proliferation.
Fig. 4.—Front view of protruding mass.

Because of the firm and protruding tumor, the mouth was kept open from angle to angle (Fig. 4), and the bulky upper lip strongly protruded (Fig. 5). It consisted of a mass of tissue 6 cm. long and 3 cm. wide, which extended from one angle of the mouth to the other and projected from the opening of the mouth. The upper part of the tumor was covered with the movable upper lip. The lip as well as the buccal soft parts were easily separated from the surface of the protruding mass. The tissue mass was located on the upper part of the gingiva; it was extremely thick at the anterior part and covered the outer surface of the teeth in the form of a gradually thinning lobe until it reached the occlusal surfaces of the premolar and molar teeth. On the inner side, the mass extended to the hard palate. The tissue proliferation was dense, elastic, and gray with a somewhat lobulated surface. The part emerging from the opening of the mouth had the consistency of soft flesh with a smooth surface that could be wrinkled. Here it was of a bluish red color with occasional brown spots. The incisor teeth were embedded in the tissue, but the cutting edges could be palpated. The extension of the tumor was about 1.5 cm. outward and inward from the crown of the teeth. The lower incisors were in labioversion. The gingiva was very thin and showed a serrated lobulation on the labial surface, which was firm and gray.

A considerable part of the tumor was removed for biopsy. One could consider this removal to be a complete extirpation in the respective area, and it was of interest that it recurred to its original size in a very short time.

Histologically, the tumor consisted of a mass of atypical vessels below the normal multilayered oral epithelium. The connective tissue was moderately

Fig. 5.—Lateral view of tumor and protruding upper lip.

Fig. 6.—Low-power photomicrograph of tissue proliferation in oral cavity. Below the normal squamous epithelium, several vessels can be detected in the connective tissue with abundant inflammatory cells. (Hematoxylin and eosin stain. Magnification, approximately ×80.)

infiltrated here and there with inflammatory cells (Fig. 6). The vessels generally had a thin wall which consisted of endothelium and no more than a thin ring of connective tissue. Their width and course were extremely irregular (Figs. 7 and 8). Orcein staining did not show elastic fibers in the vascular walls. A part of the vessels was obstructed by a loose connective tissue; other parts, however, were open and contained erythrocytes in their lumen. In view of the occurrence of vessels in such great numbers, which leads to a spongelike vascular arrangement under the mucous membrane, and the morphologic characteristics of the single vessels, it is evident that this was a diffuse angiomatous vascular proliferation which began its rapid development after the intracranial operation, that is, at a relatively late stage after birth.

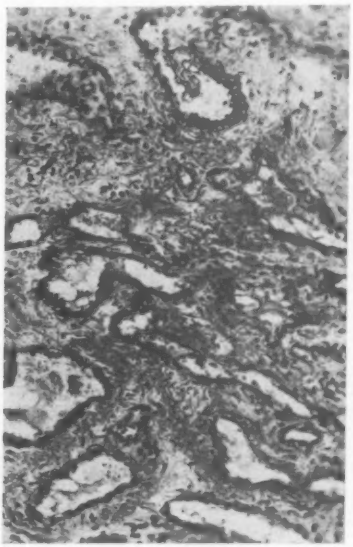

Fig. 7.

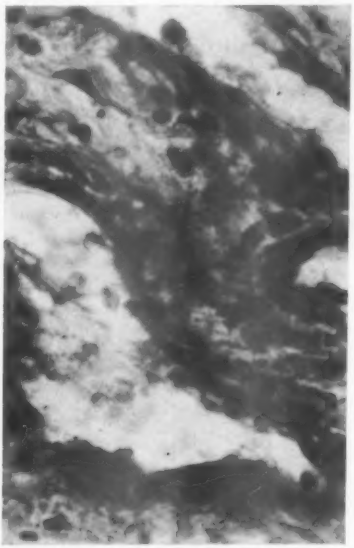

Fig. 8.

Fig. 7.—Part of the angiomatous tissue. Note mass of thin-walled, irregular-sized, partly obstructed vessels. (Hematoxylin and eosin stain. Magnification, approximately ×150.)

Fig. 8.—High-power photomicrograph of some blastomatous vessels. Note thin wall and irregular lumen. (Hematoxylin and eosin stain. Magnification, approximately ×500.)

The literature contains hints that developmental anomalies of the vessels in the brain and in the eyes give rise to symptoms only in later life. One may draw the conclusion, therefore, that the case presented here may have been an abortive one in which an abnormality of vascular development had developed in response to the operation-induced trauma. This verifies also that in these cases there exists a combined developmental disorder of the nervous and vascular systems and that this is a characteristic feature of the syndrome. Since this was the first case, according to the literature available in Hungary, in which surgical extirpation of the lobe could be performed and in which a rapidly developing postoperative vascular tissue proliferation of the gingiva took place,

it is felt that the description of this rare case with the unusual localization of the abnormal vascular tissue proliferation in the mouth should be of interest to the stomatologist.

SUMMARY

In a 13-year-old girl with Sturge-Weber's disease a rapidly developing tumor was observed located in the formerly slightly enlarged gingiva in the vicinity of the upper incisors. It grew rapidly after partial resection of the occipital brain lobe, performed because of calcifying angiomatosis (with epileptic seizures). Histologically, an angiomatous growth was demonstrated in the gingiva.

EDITORIAL NOTE

This is a rare syndrome, and it should be pointed out that cases varying in details have been reported in the American literature.*

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THE GINGIVAE

Thomas J. Cook, D.D.S., and John S. McKenzie, D.D.S.,** Miami, Fla.*

THE oral cavity is lined with mucous membrane. The membrane nearest the teeth is the gingiva, and that part of the gingiva that fills the space between the teeth is known as the interdental papilla (Fig. 1, *A*).

The gingiva, which normally is pink in color and firmly attached to the periosteum of the alveolar bone, is subjected to intrinsic and extrinsic factors more than other mucous membranes in the oral cavity. Gingivitis is a common disease. Benign and malignant tumors may originate in the gingivae, and systemic diseases are known to present oral manifestations in the gingivae.

GINGIVITIS

Inflammation of the gingiva, caused by poor oral hygiene or by bacteria, is by no means an uncommon finding, particularly in the younger age groups (Fig. 1, *B*).

The role that microorganisms play is variable, depending on their virulence and adaptability to the environment of the oral cavity as well as to the tissue tone and resistance of the host.

The diagnosis of Vincent's infection is made on the basis of clinical findings and is substantiated by microscopic study (Fig. 2).

Proper treatment, with the cooperation of the patient, can halt the process and return the gingival tissue to nearly normal.

BISMUTH STOMATITIS

The internal administration of bismuth leads to bismuth salts being absorbed into the circulating blood to form a precipitate. This precipitate combines with the hydrogen sulfide in the tissues, producing an insoluble blue "bismuth line," often confined to the gingival papilla. Patients often complain of a metallic taste. Strict oral hygiene during treatment is recommended.

UREMIC STOMATITIS

The oral manifestation of uremia is found on the gingival mucosa in patients with general body dehydration. One characteristic of diagnostic significance is a marked urine-like odor.

*Clinical Associate Professor, Division of Oral Surgery, Department of Surgery, University of Miami School of Medicine; Consultant, Oral Surgery, Veteran's Administration Hospital, Coral Gables, Florida.

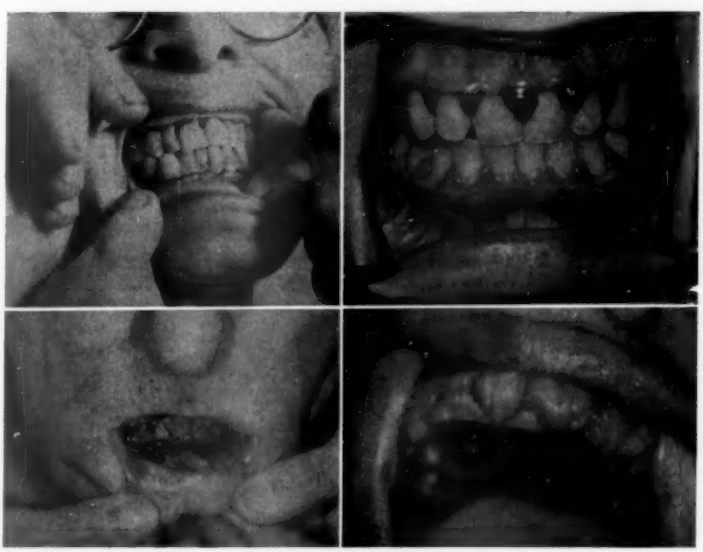
**Consultant, Periodontia, Veteran's Administration Hospital, Coral Gables, Florida.

A. Fig. 1. B.

A. Fig. 2. B.

Fig. 1.—*A*, The normal gingivae. *B*, Gingivitis.
Fig. 2.—Vincent's infection.

A. A.



B. B.

Fig. 3. Fig. 4.

Fig. 3.—*A*, Bismuth stomatitis. *B*, Uremic stomatitis (Case 1).
Fig. 4.—*A*, Pregnancy "tumor" gingivitis (Case 2). *B*, Dilantin reaction.

CASE 1.—A 68-year-old man was admitted to a local hospital on July 16, 1958, in critical condition.

History.—The patient's wife stated that her husband had been under the care of a urologist for several years because of a kidney ailment. The patient had complained of a sore mouth for several days and was taken to the family dentist. He was referred to a physician, who performed a biopsy on the same day (July 15).

On the morning of July 16 the patient collapsed in the bathroom and was brought to the hospital by ambulance.

Findings.—Oral examination made shortly after the patient's arrival at the hospital revealed a marked urine-like odor of the mouth. The gingivae on the lingual and buccal surfaces and the mucosa of the lower lip were covered with a grayish slough (Fig. 3, *B*). The urine-like odor and the gingival involvement led to a tentative diagnosis of "uremic stomatitis." General medical care was administered and the necessary laboratory work was done.

The patient died on the seventh day after admission. An autopsy was performed, the laboratory reports were assembled, and the oral diagnosis of uremic stomatitis was confirmed.

A report on the biopsy performed on the day previous to the patient's collapse indicated "acute purulonecrotic inflammation and ulceration."

Biopsy is not recommended in cases such as the one just described.

GINGIVITIS DURING PREGNANCY

The changes in the gingival mucosa of pregnant women are referred to as "pregnancy gingivitis." There may be gingival bleeding or hypertrophy of the gingivae; the gingivae are deep red in color. The tissues usually return to normal after parturition.

CASE 2.—A 24-year-old woman with the complaint of "swollen gums" was seen in consultation. The patient was in the fourth month of her first pregnancy.

History.—There had been bleeding from "the gums" during her menstrual periods since menarche. She had only three small occlusal fillings, no carious teeth, and no deposits of calculus. She took vitamins daily and used a variety of mouthwashes. In the interim between periods, there was no evidence of gingival bleeding.

The patient stated that there had been no gingival bleeding during the first sixteen weeks of pregnancy but that the gingivae had begun to "swell" two weeks previous to her visit to the office.

There was a hyperplasia of the gingivae, especially about the anterior teeth of the maxilla (Fig. 4, *A*).

When this patient was seen two months after parturition, the gingivae had returned to normal.

DILANTIN HYPERTROPHY

Dilantin (diphenylhydantoin sodium), an anticonvulsant that has proved useful in the treatment of epilepsy, has attracted our attention because of its side action, that is, involvement of the gingivae. This oral manifestation is frequently referred to as dilantin hypertrophy of the gums (Fig. 4, *B*).

The exact method by which Dilantin acts remains to be determined. It is known, however, that some of the patients receiving this drug develop a sore mouth two or three weeks after treatment is started. The soreness may then disappear and be followed by swelling of the gingivae, which bleed easily on

probing. The gingivae finally appear to become hard, firm, and more normal in color. The length of treatment seems to be a factor in that the longer a case is treated, the more pronounced is the hypertrophy.

It is known, however, that the character of the lesion is influenced by local irritation. In the clean mouth, the hyperplastic tissue is firm and smooth, but in mouths in which the hygienic condition is poor, more inflammation and bleeding may be found. This is true of other cases of reaction in the gingivae associated with systemic disorders. In patients who receive bismuth therapeutically, some of the bismuth is deposited in the marginal gingivae and appears familiarly as a blue line. In mouths with poor oral hygiene, the blue line is exaggerated and frequently a stomatitis will follow. This reaction can be reduced to a minimum by establishing strict oral hygiene.

It would seem plausible that the oral manifestation in patients receiving Dilantin could be reduced if strict oral hygiene were established before the drug is administered and, with massage of the gingivae, continued during the course of treatment.

PERIPHERAL GIANT-CELL REPARATIVE GRANULOMA

Peripheral giant-cell reparative granuloma is a benign tumor of the gingiva which has its origin in the interdental papilla or gingival margin.

The tumor is firm in consistency, has a smooth surface, and may be sessile or pedunculated in the base attachment (Fig. 5). The underlying bone may be involved, and teeth may be displaced as the tumor grows.

Fig. 5.—"Epulis."

CASE 3.—A 46-year-old waitress applied for treatment because of a "lump between the upper teeth."

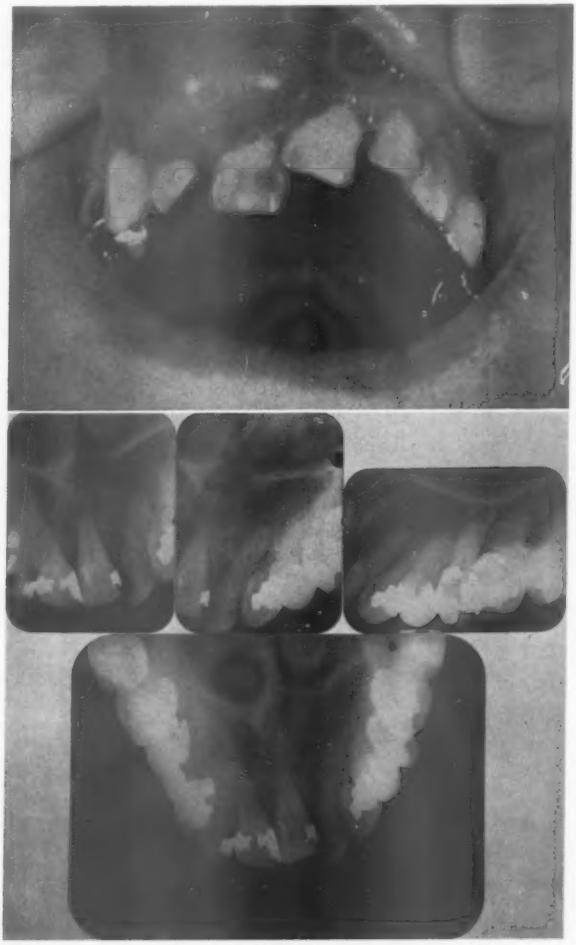
History.—The growth had started between the maxillary right first and second incisors a year previously. The patient felt that food was caught between the teeth; the area bled freely when she used a toothpick. During the past three months friends had frequently asked her what was causing her front teeth to move. She then decided to do something about it.

Findings.—Clinical examination revealed a tumor, measuring 2 by 2 cm., which extended from the gingiva into the vestibule. It was a smooth, sessile, firm mass which was slightly darker in color than the adjacent mucosa (Fig. 6, *A*). The maxillary incisors had shifted, and there was space between the right first and second incisors where the tumor had its origin.

X-ray examination revealed resorption of bone about the teeth and changes in the maxillary bone (Fig. 6, *B*).

Procedure.—The patient was admitted to Jackson Memorial Hospital, where the results of a medical checkup were reported to be within normal limits. Under local anesthesia, the tumor was removed along with the four incisors. Convalescence was uneventful, and the patient was discharged on the third postoperative day.

A.



B.

Fig. 6.—Case 3. *A*, Peripheral giant-cell reparative granuloma. *B*, Radiographs reveal resorption of bone between the maxillary incisors and areas of trabeculation in the maxillary bone.

The pathologist's report indicated "peripheral giant-cell reparative granuloma."

A partial denture was inserted to replace the missing teeth. A checkup four years later revealed that there has been no recurrence.

CASE 4.—A 10-year-old Negro girl was seen in the oral surgery clinic at Jackson Memorial Hospital.

History.—The mother stated that the child had normal deciduous teeth but "the gums became swollen and the baby teeth fell out." Little attention was paid to the child until she complained of not being able to chew "because the upper teeth cut into the lower gum."

Findings.—A tumor mass occupied the area from the first molar on the right side to the cuspid area on the left. It extended into the vestibule and onto the lingual surface. The permanent incisors were missing on the right side, while those on the left had shifted. Two areas on the right side showed the imprint of the maxillary teeth (Fig. 7, *A*).

Fig. 7.—Case 4. *A*, Peripheral giant-cell reparative granuloma in a 10-year-old child. *B*, Radiograph reveals the permanent incisors displaced to the left and expansion of the mandible with rarefaction.

X-ray examination revealed a tumor mass which contained what appeared to be both cystic and bone formation. There were unerupted permanent teeth on the right and displaced teeth on the left (Fig. 7, *B*).

Procedure.—The patient was admitted to Jackson Memorial Hospital, where physical examination and laboratory studies revealed a healthy child of 10 years.

Under general anesthesia, the tumor mass was removed along with the affected teeth on the left side. The unerupted teeth on the right were not disturbed. Convalescence was uneventful.

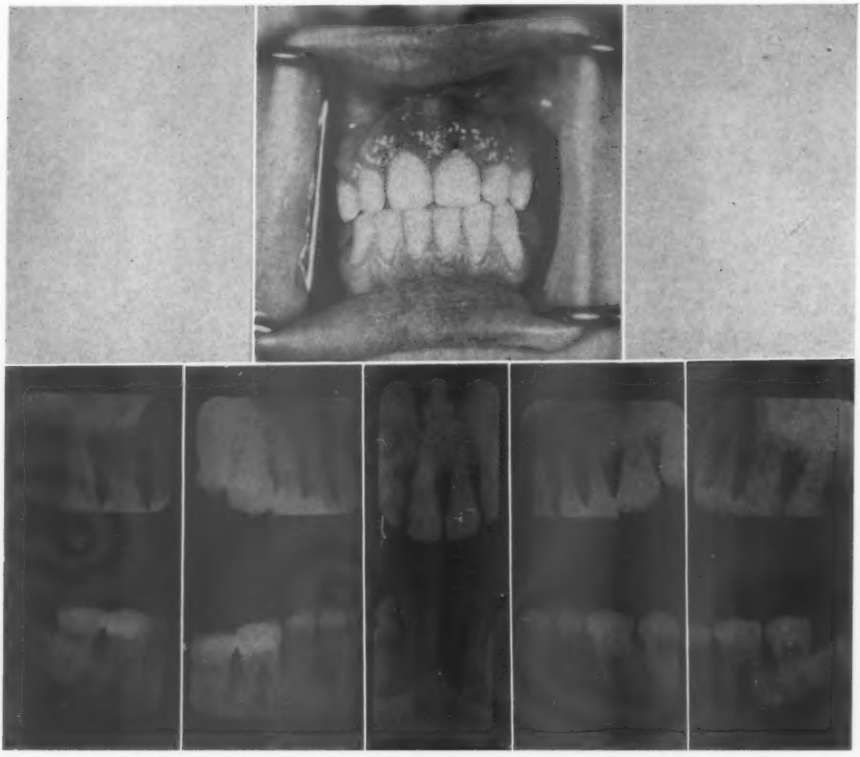
This child has been seen periodically over the years, and there has been no recurrence of the tumor.

The pathologist's report was "giant-cell tumor, benign."

DIABETES

Diabetes is a metabolic disease in which signs and symptoms are manifested in the oral cavity. If the insulin manufactured by the body is inadequate to burn completely the carbohydrates of the diet, the sugar that is not burned accumulates in the blood. When this reaches a certain level, it is "spilled over" into the urine. When this occurs, as revealed by increased blood sugar determination and the presence of sugar in the urine, the patient is said to have diabetes.

A.



B.

Fig. 8.—Case 5. *A*, Gingival inflammation in a diabetic patient. *B*, Roentgenograms reveal destruction of alveolar bone.

In patients with uncontrolled diabetes the gingival mucosa may become inflamed and ulcerated. There is extensive loss of alveolar bone, and the teeth are loose.

CASE 5.—An attractive 21-year-old white woman applied to an airline company for a position. Routine physical disclosed that she had diabetes. The teeth were in good repair

and appearance; the gingivae were spongy and bled easily (Fig. 8, *A*). Dental x-ray examination revealed a marked loss of alveolar bone about each tooth (Fig. 8, *B*). The patient stated that she had had "bleeding gums" for over a year but had been told it was due to a vitamin deficiency.

GRANULOMA PYOGENICUM

Granuloma pyogenicum or capillary hemangioma, granular type, may have its origin in and about the gingiva. It is usually a protruding mass, often the result of trauma, and bleeds readily. Complete surgical excision will affect a cure (Fig. 9, *A*).

Fig. 9.—*A*, Granuloma pyogenicum. *B*, Carcinoma.

CARCINOMA

In cancer of the gingival mucosa, particularly when teeth are present, secondary infection leads to ulceration (Fig. 9, *B*). There may be invasion of the cancer into the mandible, the teeth become loosened, and there is marked fetor oris.

In suspicious cases a biopsy should be performed before any teeth are removed. It appears that when teeth are removed the tumor spreads rapidly. A patient frequently remarks, "I was all right until a tooth was removed."

BLOOD DYSCRASIAS

Accumulated evidence from patients with blood dyscrasias indicates that in many instances symptoms appear in the gingivae as the first sign of disease. Gingival hypertrophy is found in leukemia, and hemorrhage from the gingiva is seen in cases of purpura.

Fig. 10.

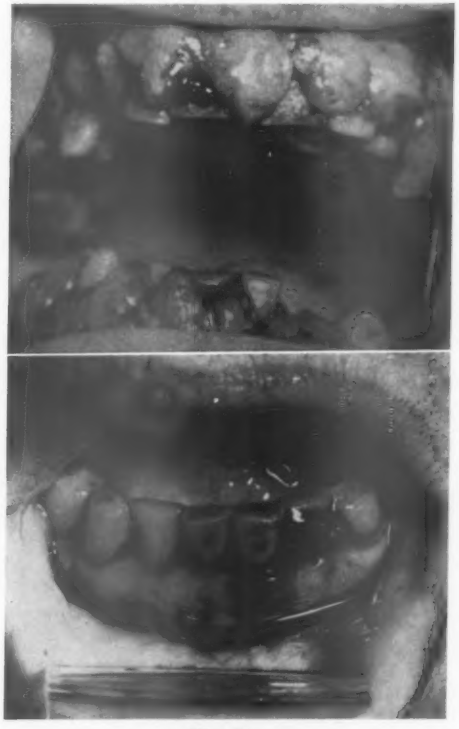


Fig. 11.

Fig. 10.—Case 6. Leukemia.
Fig. 11.—Thrombocytopenic purpura hemorrhagica.

Leukemia is a progressively fatal disease, characterized by a widespread hyperplasia of the hematopoietic tissues resulting in the production of excessive numbers of immature white cells, which either circulate in the blood stream, become deposited in the fixed tissues, or both.

CASE 6.—Patient R. C., a 52-year-old married man, a contractor, applied for treatment at the Oral Diagnosis Clinic, School of Dentistry, University of Pennsylvania. Although the patient could afford to pay the regular fee, his physician suggested that he go to the dental school for his extractions because "his case was out of the ordinary."

Previous History.—One month previously, the patient felt somewhat unwell; he fatigued easily and was neglecting his business. He lost his appetite because his "gums were sore." His family physician prescribed a tonic.

During the next two weeks, the patient lost several pounds in weight, and he felt that "the infection was spreading in [his] gums and that [his] breath was awful."

Findings.—The general condition of the mouth was unhygienic. This condition was no doubt due to the fact that the patient was unable to brush his teeth. The gingivae were tender, bluish red, somewhat hypertrophied generally, and bled easily (Fig. 10).

A blood count revealed the following:

Red blood cells	2,800,000
White blood cells	205,000
Platelets	14,500
Hemoglobin	46 per cent
Polymorphonuclear leukocytes	12 per cent
Lymphocytes	2
Monocytes	0
Eosinophils	1
Myelocytes	16

The patient's family was advised of his condition, and arrangements were made for his admission to the hospital, where a diagnosis of acute leukemia was made. Medical treatment included blood transfusions and supportive measures. At the end of a month the patient felt better and had gained several pounds. Along with the general improvement, the general condition of the gingival tissues was better, the bleeding had stopped, and the areas of ulceration seemed to respond to the general medical treatment and oral hygiene. The patient was permitted to return to his home after a month in the hospital and was then followed as an outpatient.

In less than a month the patient became acutely ill and was readmitted. There was a marked gingival hypertrophy, with extensive areas of necrosis throughout. The gingivae bled easily, and it became difficult to give relief even for the marked fetor oris.

The course of the disease continued in spite of medical treatment. As the disease progressed, the general appearance of the gingivae became worse until the hypertrophied gingivae extended to the incisal edges of the teeth and there was finally a generalized necrosis. The patient died.

At autopsy, the gingivae exhibited a remarkable grayish green, hemorrhagic, fleshy, friable thickening which extended down over and completely covered the teeth. The histologic diagnosis of the gingivae was "leukemic infiltration, marked."

Thrombocytopenia purpura hemorrhagica is a dyscrasia in which there is a marked decrease in platelets, and hemorrhage from the gingival margin is found (Fig. 11).

COMMENT

The gingival mucous membrane may manifest lesions that are local in character or that represent the oral manifestations of systemic disease.

The cardinal principle for the successful treatment of disease in any part of the body is correct diagnosis; naturally, the same is true of gingival lesions.

JACKSON MEMORIAL HOSPITAL

PHARMACOLOGY AND THERAPEUTICS

USE OF BUCCAL STREPTOKINASE IN THE TREATMENT OF INFECTION AND EDEMA

John M. Hyson, Jr., D.D.S., M.S., Baltimore, Md.*

THE dental profession has always been interested in the treatment and control of edema encountered in oral surgery. Many drugs have been studied as possible solutions to this problem. Streptokinase has received favorable reports.

In 1949 the beneficial use of streptokinase and streptodornase in the treatment of fibrinous, purulent, and sanguineous pleural effusions was reported.[1] The effective local use of streptokinase and streptodornase in the treatment of an infection of the neck secondary to a dentoalveolar abscess was noted in 1951.[2] A case in which an antro-oral fistula, which followed extraction of a maxillary second molar, was successfully treated with streptokinase-streptodornase irrigations and antibiotic therapy was reported in 1952.[3] In 1953, good results from the use of Varidase (streptokinase-streptodornase) in various dental infections were noted.[4] In 1954, a case in which osteomyelitis of the canine fossa was treated successfully with streptokinase-streptodornase irrigations was reported.[5]

In 1955 the intramuscular injection of Varidase in the treatment of infection and edema was reported,[6] beneficial results being obtained within two days after therapy was begun. The intramuscular injection of pure streptodornase or hyaluronidase failed to produce a good therapeutic effect. Streptokinase was therefore thought to be the active therapeutic agent in Varidase.

Two cases of postoperative edema following extraction of teeth were successfully treated with intramuscular streptokinase in 1958.[7]

Although good results were obtained with streptokinase, the methods of administration left much to be desired. Streptokinase had to be administered either as a local irrigation or as an intramuscular injection twice a day from

Based upon a thesis submitted in partial fulfillment of the requirements for the degree of Master of Science, Graduate School, University of Maryland.

*Formerly instructor in the Department of Oral Surgery, Baltimore College of Dental Surgery, Dental School, University of Maryland.

a freshly prepared solution. It was not very practical for use in dental patients unless the patients were hospitalized.

In 1958 the use of a buccal preparation of streptokinase-streptodornase (Varidase—Lederle) which produced therapeutic results similar to those produced by the intramuscular preparation was reported.[8] This work was confirmed the same year.[9] Immunologic evidence of mucosal penetration was obtained in ten of fourteen patients.

The buccal tablet offered a convenient method of administering streptokinase to the dental patient either as a prophylactic measure to prevent edema in traumatic oral surgical procedures or as a therapeutic measure in the treatment of infection and edema.

In October, 1957, the initial clinical study was begun on the therapeutic use of buccal Varidase in patients with swellings due to trauma or infection who sought treatment at the Dental Surgery Clinic of the Out-Patient Department of University Hospital.

Those patients with a history of rheumatic fever, rheumatoid arthritis, or a severe clotting defect were excluded from the study. Streptokinase could cause an allergic reaction in patients with a history of one of the collagen diseases. Because of the possibility of hemorrhage, it should not be given to patients with defects in the clotting mechanism. The administration of streptokinase is also contraindicated in patients with extensive liver damage, acute hemorrhagic pancreatitis, acute renal insufficiency, and afibrinogenemia, since the clotting mechanism may be impaired in these diseases.

Buccal Varidase is a concentrated and partially purified protein preparation which contains streptokinase and streptodornase with some hyaluronidase and ribonuclease. In tablet form, this preparation dissolves easily in the mouth.

The tablets used in this study contained 20,000 units of streptokinase. The dose was one tablet every twelve hours, and instructions to the patient were as follows:

1. Place the tablet in either side of the buccal vestibule.
2. Allow the tablet to dissolve in two to five minutes.
3. Do not swallow the saliva for five minutes after the tablet is completely dissolved.
4. Do not expectorate for five minutes after the tablet is dissolved.
5. Do not swallow the tablet.

All patients were also given 250 mg. tetracycline hydrochloride tablets (Achromycin—Lederle). The dose of the antibiotic was 0.5 Gm. initially and then 0.25 Gm. every six hours. If infection was severe, the dose was increased to 2 Gm. daily.

Photographs were secured at the initial visit, if possible, and at the times of subsequent treatments to record the edema visible externally. Temperature records were kept for all patients. In all cases, observations were made on the progress of infection, edema, and healing. Extraction, incision and

drainage, wiring, or other indicated surgical procedures were carried out when indicated. No other medication was given unless an analgesic was necessary for pain.

Results were graded as excellent, good, or poor according to clinical judgment based on the rate of reduction of the edema and the healing.

In the period from Oct. 22, 1957, to July 1, 1958, twenty-five patients with swellings due to diseases of dental origin were treated with buccal Varidase and tetracycline. Of these, nine patients failed to return after the initial treatment; thus, the results were based on the remaining sixteen cases. Table I shows the results in these cases plus one other treated at a later date.

TABLE I. RESULTS OF TREATMENT WITH BUCCAL VARIDASE AND TETRACYCLINE

CONDITIONS TREATED	NO. OF CASES	RESULTS		
		EXCELLENT	GOOD	POOR
Abscess	5	5	–	–
Cellulitis	10	5	4	1
Fractured mandible	1	1	–	–
Fractured zygoma	1	1	–	–
Totals	17	12	4	1

Treatment was successful in all but one of the seventeen cases. Reduction of edema and healing were excellent. No aggravation of infection was seen in any of the patients. Pain and tenderness in the mouth and sore throat did not occur. No chills, cyanosis, hemorrhage, formation of hematomas or petechiae, or allergic reactions were noted. Temperature elevations which might have been attributable to the drug were recorded in only two of the seventeen patients, and in both of these the temperature elevations were less than 1.0° F. Four patients in whom previous antibiotic therapy for periods ranging from two to six days had been unsuccessful showed dramatic improvement when given buccal Varidase. The patients' ages ranged from 15 to 66 years. The number of days of therapy varied from three to fourteen. Three of the resistant patients treated had positive serologic tests for syphilis.

From the study, the following conclusions were made:

1. Buccal Varidase in conjunction with antibiotic therapy is very effective in the treatment of infection and edema.
2. Buccal Varidase is a safe drug. No drug reactions were encountered.

A new project was set up on a double-blind basis, so that neither the patient nor the surgeon would know whether the patient was receiving streptokinase or a placebo at the time of treatment. A placebo that exactly resembled the buccal Varidase tablet was made by the Lederle Laboratories. Fifty patients' charts were printed and numbered from 1 to 50. Fifty envelopes were also numbered from 1 to 50 and stamped with the same instructions for taking the buccal tablet as in the previous study.

Twelve tablets of buccal Varidase were placed in each of twenty-five envelopes selected at random. Each tablet contained 10,000 units of streptokinase. Twelve buccal placebo tablets were placed in each of the remaining twenty-five envelopes.

A master code sheet was made, on which were listed the numbers of the twenty-five envelopes with Varidase and the twenty-five that contained the placebo. The corresponding charts and envelopes were stapled together. By comparing the number on the patient's chart with the master code sheet, it was possible to determine which drug the patient had received once treatment was completed and results were recorded.

In addition, another envelope containing twenty-five 250 mg. tablets of tetracycline (Achromycin—Lederle) was stapled to each patient's chart. Directions were stamped as follows: "One tablet after each meal and at bedtime (four tablets a day total)." No code number was placed on this envelope, since all patients were to receive the antibiotic drug.

The dose of the buccal Varidase 10,000 unit tablet (or placebo) was one tablet twice a day. The dose of tetracycline was two 250 mg. tablets initially and then 1 Gm. daily by the oral route. The envelopes thus contained a six-day supply of each drug.

TABLE II. RESULTS OF TREATMENT WITH BUCCAL VARIDASE AND TETRACYCLINE (DOUBLE-BLIND EXPERIMENT)

CONDITIONS TREATED	NO. OF CASES	RESULTS		
		EXCELLENT	GOOD	POOR
Abscess (dentoalveolar)	8	6	2	-
Cellulitis	3	3	-	-
Fractured mandible	3	1	2	-
Hematoma	1	-	1	-
Postoperative edema	1	1	-	-
Totals	16	11	5	0

When a patient with a swelling presented himself, one of the coded charts would be selected and filled out. Edema would be recorded, on the basis of clinical judgment, as severe, moderate, slight, or none. The patient was then given both drug envelopes (Varidase or placebo and tetracycline) with instructions to follow the directions closely. Two tablets of tetracycline and one buccal tablet were given at the initial visit. The patients were observed daily or on alternate days, and the amount of edema was noted. Any abnormal reaction was also recorded. Any indicated surgical procedures, such as incision and drainage, change of dressings, extractions, and reduction and fixation of fractures, were done. No other medication was given to the patient unless an analgesic was necessary for severe pain. If the severity of the infection necessitated longer treatment, the patient was continued on the antibiotic drug but not on the enzyme. At the completion of treatment the results were recorded for each patient, on the basis of clinical judgment, as excellent, good, or poor.

From Sept. 24, 1958, to March, 1959, a total of twenty-seven patients were treated in the prescribed manner. Sixteen patients received the buccal streptokinase, and eleven patients received the buccal placebo. In addition to these, twelve patients (seven given Varidase and five given the placebo) failed to return for treatment after the first or second visit and were not included in the results. Table II shows the results of the buccal streptokinase therapy.

TABLE III. RESULTS OF TREATMENT WITH BUCCAL PLACEBO AND TETRACYCLINE (DOUBLE-BLIND EXPERIMENT)

CONDITIONS TREATED	NO. OF CASES	RESULTS		
		EXCELLENT	GOOD	POOR
Abscess (dentoalveolar)	6	2	3	1
Cellulitis	4	2	1	1
Fractured mandible	1	-	-	1
Totals	11	4	4	3

Table III shows the results of buccal placebo therapy.

No reactions, local or systemic, occurred with either buccal tablet. No allergic reactions to tetracycline were encountered, and no fever, chills, cyanosis, hemorrhage, hematomas, or petechiae were noted. No prolonged hemorrhage following surgery was observed.

A study of the results of this project indicated that in general the patients who received the Varidase had a shorter recovery period than those given the placebo. This fact was evidenced by an improved rate of edema reduction and clinical improvement. This study confirmed the earlier conclusion that buccal Varidase is an effective and safe drug for use by the patient who needs oral surgery. The combination of buccal Varidase and an antibacterial drug is an excellent addition to the dental drug armamentarium.

Fig. 1. Fig. 2.

Fig. 1.—Traumatic injury to face. Fractured zygoma.
Fig. 2.—Twenty-four hours after start of buccal Varidase and tetracycline therapy.

CASE REPORTS

CASE 1.—A 35-year-old woman reported to the Accident Room of University Hospital on Feb. 17, 1959, with a severely swollen face caused by a kick in the face. She had a swelling of the left maxillary area and lip, complete closure of the left eye by edema, nasal hemorrhage, and a buccal hematoma. The roentgenogram revealed a fracture of the

left zygoma. The patient was given 600,000 units of penicillin, and a petrolatum gauze pack was inserted in the left nostril. On February 18 the patient reported to the Out-Patient Department for treatment (Fig. 1). She was placed on buccal Varidase, 10,000 units every eight hours, and tetracycline, 0.25 Gm. orally every six hours. When the patient

Fig. 3. Fig. 4.

Fig. 3.—Five days after start of buccal Varidase and tetracycline therapy.
Fig. 4.—Thirteen days after start of buccal Varidase and tetracycline therapy.

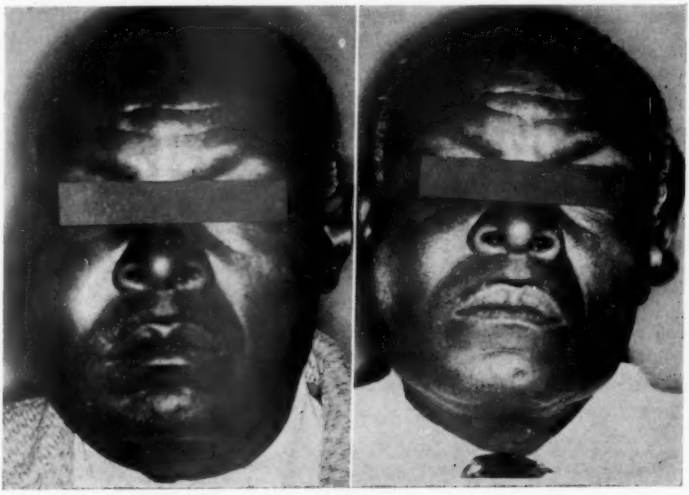


Fig. 5. Fig. 6.

Fig. 5.—Cellulitis of the right side of the face.
Fig. 6.—Five days after start of buccal Varidase and tetracycline therapy.

returned on February 19 there was less edema about the left eye (Fig. 2). On February 20 the facial edema had decreased considerably. On February 23 about 5 c.c. of old blood was aspirated from the swelling (Fig. 3). The patient showed continued improvement on February 26, and the residual swelling was fairly hard. On February 28 all medication was discontinued. The patient was transferred to the Otolaryngology Department on March 4, with only a slight hard swelling over the fracture site (Fig. 4).

CASE 2.—A 49-year-old man reported to the Oral Surgery Department of the University of Maryland School of Dentistry on March 4, 1959, with a severe swelling of the right face and submaxillary region (Fig. 5). Tetracycline, 0.5 Gm., and buccal Varidase, 10,000 units, were administered on admission, and the patient was placed on tetracycline, 0.25 Gm. orally every six hours, and buccal Varidase, 10,000 units every twelve hours. On March 6, 1959, he returned with less facial edema. Improvement continued, and on March 9 the maxillary right second and third molars were extracted under local anesthesia (Fig. 6). The patient was discharged on March 10, with no edema.

CONCLUSION

Two separate studies on the clinical use of buccal Varidase in the treatment of infection and edema were made. Both the preliminary and the double-blind studies produced similar results. Edema resolution and healing were excellent in most cases. No unusual postoperative hemorrhage was noted in any patient. No allergic reactions or local irritations following administration of the buccal tablet were reported. Buccal Varidase, therefore, was found to be a safe and valuable drug in the treatment of edema in oral surgery.

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ORAL ROENTGENOLOGY

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THE NORMAL GLUCOSE-TOLERANCE PATTERN

Development of Blood Glucose Normality by an Analysis of Oral Roentgenographic Findings

E. Cheraskin, M.D., D.M.D., and L. Manson-Hing, D.M.D.,***
Birmingham, Ala.

INTRODUCTION

THERE is still considerable debate as to what should be regarded as the *normal* glucose-tolerance pattern. The presently accepted range has been developed by an analysis of *presumably* healthy persons. A report has already been released[1] in which the glucose-tolerance pattern in a group of dental patients with and without *oral* symptoms has been analyzed. The symptoms studied (gingival tenderness, stomatopyrosis, and xerostomia) were those which are ordinarily recognized as being common findings associated with diabetes mellitus.

A second report[2] has also been released in which the glucose-tolerance pattern in a group of dental patients with and without *extraoral* symptoms has been analyzed. The symptoms studied (polyphagia, polyuria, and polydipsia) were those ordinarily regarded as being common findings in the diabetic patient. There is also in preparation a series of reports designed to analyze the glucose-tolerance pattern in a group of dental patients with and without *oral signs* generally regarded as common findings in patients with diabetes mellitus. For example, reports are in preparation regarding the relationship of carbohydrate imbalance to gingival findings,[3] lingual signs,[4] and dental clues.[5]

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*Professor and Chairman, Section on Oral Medicine, University of Alabama School of Dentistry.

**Fellow in Oral Medicine, University of Alabama School of Dentistry; member, American Academy of Oral Roentgenology.

The present report will attempt to analyze the relationship between the glucose-tolerance patterns in patients with and without *roentgenographic findings* generally considered to be associated with the diabetic state.

REVIEW OF THE LITERATURE

In order that the design and results of this study might be appreciated, it is necessary to review briefly (1) the common oral roentgenographic findings associated with diabetes mellitus and (2) the present basis for the so-called normal glucose-tolerance pattern.

Oral Roentgenographic Findings.—The two most commonly reported oral roentgenographic signs believed to be associated with diabetes mellitus are (1) periodontal widening and (2) alveolar bone loss.

Periodontal widening: Rutledge[6] observed marginal periodontal widening in fourteen of the twenty diabetic children in his series. Rudy and Cohen[7] also noted this roentgenographic finding. On the other hand, Ziskin, Siegel, and Loughlin[8] could not demonstrate marginal periodontal widening in their series of cases. Sheridan and his group[9] observed minimal to severe marginal periodontal widening in 63 per cent of their series of patients with diabetes mellitus. In contrast, only 39 per cent of the nondiabetic group demonstrated this same roentgenographic finding.

Alveolar bone loss: Rudy and Cohen,[7] Kaplan,[10] Pollack, Person, and Knishkowy,[11] Stahl,[12] Golomb,[13] Martinez,[14] and Person[15] have claimed that diabetes mellitus is associated with increased alveolar bone loss. Rudy and Cohen,[16] in a subsequent report, disagreed with their own earlier report and claimed no bone loss. Rutledge[6] observed bone loss in ten of the twenty children in his group. Lovestedt and Austin[17] have claimed that there was no significant roentgenographic difference in a group of 503 diabetic and 1,023 nondiabetic patients. Sheridan and his co-workers[9] observed no diabetic patient with normal septal crests. They found, for example, that in 54 per cent of the diabetic patients one-half or more of the alveolar support was lacking. In contrast, they noted a similar roentgenographic pattern in 34 per cent of their nondiabetic subjects.

Normal Glucose-Tolerance Pattern.—There are two general approaches for establishing normal values[18]: (1) statistical analysis and (2) physiologic analysis.

Statistical analysis: In general, the values for the normal glucose-tolerance pattern have been derived from examination of *presumably* healthy persons. In most cases, subjects have been regarded as well if they were relatively asymptomatic. Mosenthal and Barry[19] have published a set of values which are now generally regarded as the normal glucose-tolerance pattern. Their conclusions have been based upon the findings in fifty ambulatory hospital workers. These investigators suggest that the normal glucose-tolerance test is represented by a fasting venous true blood glucose level of 100 mg. per cent or less, no venous blood glucose level greater than 150 mg. per cent, and

a return of the blood glucose level to 100 mg. per cent or less at the end of two hours. Fig. 1 shows specific mean values obtained by Mosenthal and Barry in their study.

Physiologic analysis: There is no published report available which attempts to analyze the normal glucose-tolerance pattern on the basis of the absence or presence of oral roentgenographic signs which are commonly associated with diabetes mellitus.

METHOD OF INVESTIGATION

One hundred dental patients were studied in the Section on Oral Medicine at the University of Alabama School of Dentistry. As far as possible, the subjects were selected at random. Table I shows the age distribution of the group. It can be observed that the pattern approaches a typical unimodal curve. Included in this study were twenty-two male patients and seventy-eight female patients.

TABLE I. AGE DISTRIBUTION

AGE GROUP	TOTAL NUMBER OF PATIENTS
0-9	1
10-19	9
20-29	19
30-39	27
40-49	19
50-59	17
60-69	8
Total	100

Each subject was carefully examined with regard to marginal periodontal widening and alveolar bone loss by means of roentgenograms of the upper and lower anterior teeth taken by the long-cone technique. The scoring for periodontal widening was made on a three-point scale. Zero was assigned when there was no marginal widening. The values 1 and 2 were used to indicate minimal and severe marginal widening, respectively. Alveolar bone pattern was graded on a six-point scale. Zero was assigned to indicate normal septal crest. Values 1 and 2 were recorded for minimal and minimal-to-moderate bone loss. The designation 3 was utilized to indicate the loss of one-half the alveolar bone support. Values 4 and 5 were used to demonstrate moderate-to-severe and no alveolar bone support, respectively.

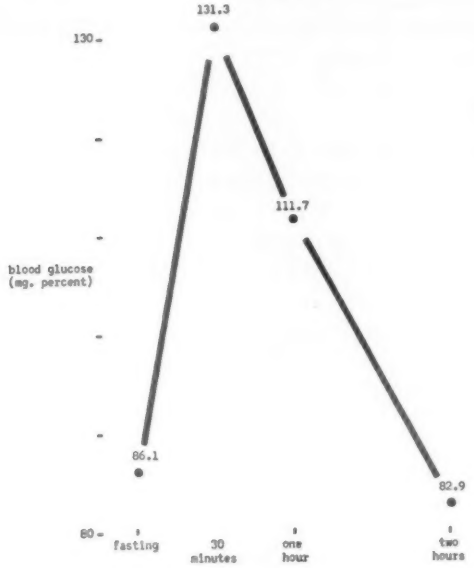
A true glucose-tolerance test was performed on each patient, according to the methods of Somogyi[20, 21] and Nelson.[22] No preparatory diet was recommended, except for complete fasting for twelve hours prior to the laboratory examination. Complete details regarding the method of investigation are available in the article by Sheridan and his group.[9]

RESULTS

The findings will be reported in two ways: (1) general characteristics of the entire group and (2) subgroup analysis.

General Characteristics.—Fig. 1 pictorially represents the normal glucose-tolerance pattern derived by Mosenthal and Barry from a study of fifty presumably healthy hospital workers. Fig. 2 summarizes the data obtained from

Fig. 1.



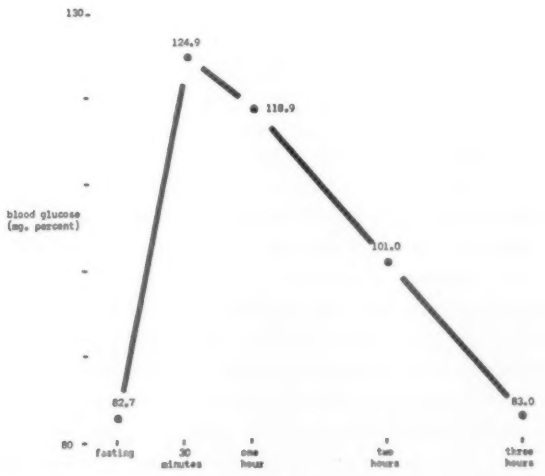


Fig. 2.

Fig. 1.—Normal glucose-tolerance pattern (according to Mosenthal and Barry.)
Fig. 2.—Glucose-tolerance patterns in 100 routine dental patients.

a study of 100 routine dental patients. Fig. 3 is a composite graphic analysis of the findings in the fifty hospital workers in the Mosenthal and Barry series and the 100 dental patients in the Alabama study. The small mean difference at the fasting level, thirty- and sixty-minute points in the two groups, is not statistically significant ($p > .200$) as outlined in Table II. The only point at which there is a statistically significant difference of the means is at two hours ($p < .005$).

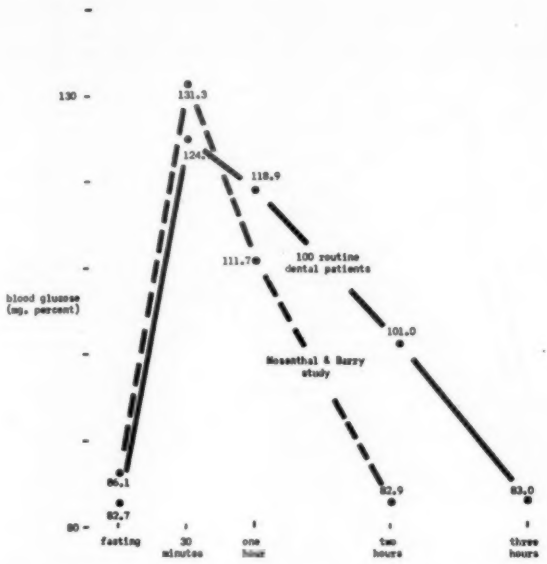


Fig. 3.—Comparison of the glucose-tolerance patterns of 100 routine dental patients with the findings of Mosenthal and Barry.

TABLE II. STATISTICAL COMPARISON OF MEAN DIFFERENCES

		BLOOD GLUCOSE DIFFERENCES				
		FASTING	30 MINUTES	1 HOUR	2 HOURS	3 HOURS
Mosenthal and Barry study versus Alabama study	Mean difference	3.400	6.400	7.200	18.100	
	P	> .200	> .200	> .200	< .005	
Periodontal widening versus no periodontal widening	Mean difference	8.400	13.600	14.100	21.600	12.100
	P	> .100	> .100	> .200	> .050	> .200
Alveolar bone loss versus no alveolar bone loss	Mean difference	7.100	8.400	26.000	28.000	13.200
	P	> .050	> .200	< .005	< .005	> .100
Alveolar bone loss and periodontal widening versus no alveolar bone loss and no periodontal widening	Mean difference	12.600	10.300	30.200	40.600	18.500
	P	< .025	> .200	< .025	< .001	> .100

Subgroup analysis.—The roentgenographic signs studied will be analyzed as (1) independent and (2) combination groups.

Single factors: Two oral roentgenographic findings were analyzed: (1) periodontal widening and (2) alveolar bone loss.

Periodontal widening. The 100 patients in the Alabama series were divided into two groups: (1) those who demonstrated periodontal widening and (2) those who did not have this particular roentgenographic finding. Eleven of the patients were edentulous and one was unrecorded; therefore, they were not included in this analysis. Of the remaining eighty-eight, forty-seven showed no periodontal widening and forty-one demonstrated this particular finding.

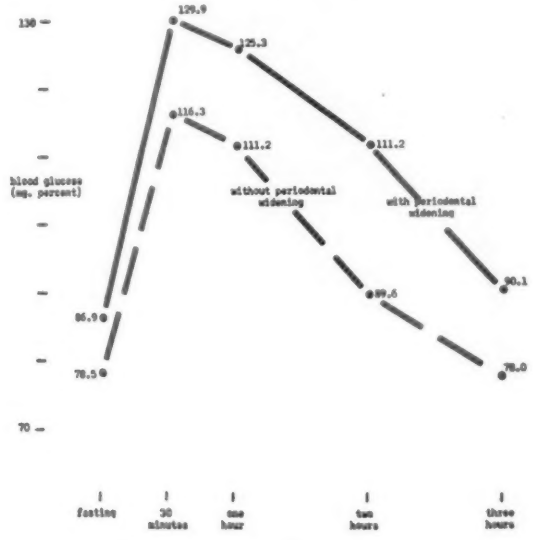


Fig. 4.—Comparison of glucose-tolerance patterns of patients with and without periodontal widening.

Fig. 4 shows the glucose-tolerance patterns obtained from these two groups on the basis of the presence or absence of this one roentgenographic clue. Five points deserve comment. First, the glucose-tolerance pattern of the group with periodontal widening suggests a decrease in tolerance as compared with the group without periodontal widening. Second, in the main, the mean differences are relatively small throughout. Third, the greatest mean difference occurred at the two-hour point. Fourth, the mean three-hour blood glucose score for the group without periodontal widening is approximately the same as the initial glucose value. In contrast, the mean three-hour blood glucose level in the patients with periodontal widening is higher than that observed initially. Fifth, it is clear from Table II that there is no statistically significant difference between these two groups at any of the temporal points.

Alveolar bone loss. The 100 patients in the Alabama series were divided into three groups: (1) those with no teeth, (2) those with no alveolar bone loss, and (3) those with evidence of alveolar bone loss. Twelve of the patients were edentulous and therefore were not included in this analysis. Of the remaining eighty-eight, eleven showed no alveolar bone loss and seventy-seven demonstrated this particular finding. Fig. 5 shows the glucose-tolerance patterns obtained from these two groups on the basis of the presence or absence of this particular roentgenographic sign. Five points deserve comment. First, the glucose-tolerance pattern of the group with alveolar bone loss suggests a decrease in tolerance as compared with the group without alveolar bone loss.

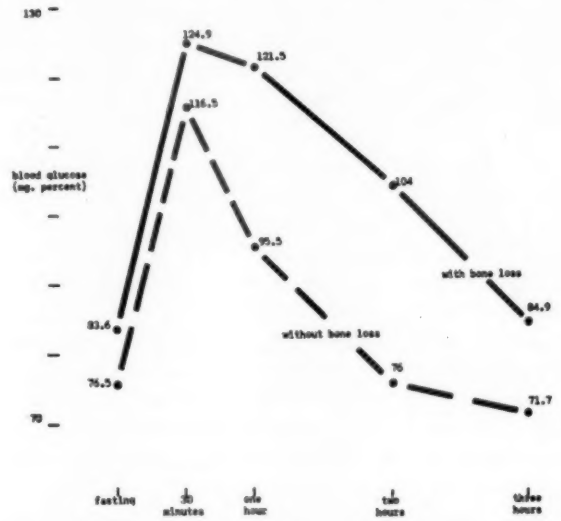


Fig. 5.—Comparison of glucose-tolerance patterns of patients with and without alveolar bone loss.

Second, in the main, the mean differences are considerably larger than those observed in the analysis of periodontal widening. Third, the greatest mean difference occurred at the two-hour point. Fourth, the mean three-hour blood glucose score for the group without alveolar bone loss is below the initial glucose finding. In contrast, the three-hour blood glucose level in the patients with alveolar bone loss is slightly higher than that observed initially. Fifth, it is clear from Table II that there is a statistically significant difference ($p < .005$) between the groups, as shown by the values at one and two hours.

Combination factors: An analysis was also made of the combination of periodontal widening and alveolar bone loss. Ten patients showed no periodontal widening and no alveolar bone loss. In contrast, forty patients demonstrated the presence of both of these findings. Fig. 6 shows the glucose-tolerance patterns obtained from the two groups on the basis of the presence

or absence of these two roentgenographic findings. Five points deserve mention. First, the glucose-tolerance pattern of the group with positive roentgenographic findings suggests a decrease in tolerance as compared with the group without these findings. Second, in the main, the mean differences are greater than previously observed from an analysis of the single roentgenographic factors. Third, the greatest mean difference occurred at the two-hour point. Fourth, the mean three-hour blood glucose score for the group without roentgenographic findings is less than that observed initially. In contrast, the mean three-hour

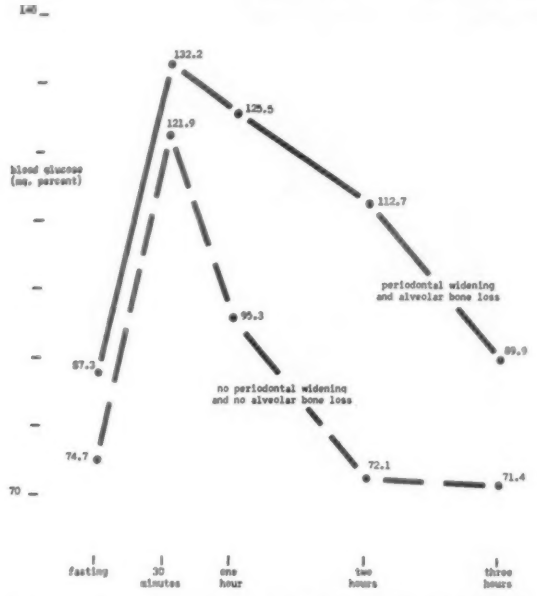


Fig. 6.—Comparison of glucose-tolerance patterns of patients with and without periodontal widening and alveolar bone loss.

blood glucose value for the patients with both of these roentgenographic findings is higher than that observed initially. Fifth, it is clear from Table II that there is a statistically significant difference between these two groups as demonstrated by the fasting ($p < .025$), one-hour ($p < .025$), and two-hour ($p < .001$) findings.

DISCUSSION

The data will be analyzed in three different ways: (1) a group analysis by comparison of the findings by Mosenthal and Barry with those observed in this study, (2) a subgroup analysis on the basis of the two roentgenographic signs studied in this series, and (3) a discussion of the findings obtained in the light of other factors (for example, age, number of teeth, and calculus) ordinarily regarded as etiological determinants in the production of periodontal widening and alveolar bone loss.

Group Analysis.—It should be recalled that the present standards for the normal glucose-tolerance curve include a fasting blood glucose of less than 100 mg. per cent, no blood glucose level greater than 150 mg. per cent, and a return to below 100 mg. per cent in two hours. On the basis of these criteria, two possibilities can be entertained. If all the above specifications must be met for normal or abnormal glucose tolerance, then the dental patients in this survey cannot be regarded as systemically healthy. This conclusion follows from the fact that significant differences between the Alabama and Mosenthal and Barry groups were observed at the two-hour period (Table II and Figure 3). If, on the other hand, normality and abnormality are to be judged on the basis of single blood glucose criteria, then the dental patients must be regarded as either well or ill, depending upon the specific yardstick employed. For example, on the basis of the fasting, thirty-minute, and sixty-minute determinations, the dental patients meet the specifications for normality. According to the two-hour determinations, however, the dental patients satisfy the requirements for systemic illness.

Subgroup Analysis.—It is noteworthy that, with regard to *single* roentgenographic findings, only alveolar bone loss appears to distinguish the diabetic from the nondiabetic patient (Fig. 5 and Table III). In this connection, it should be recalled that significant differences between those with and those without alveolar bone loss were observed at the one-hour and two-hour determinations. We should also mention that the two-hour reading for those patients with alveolar bone loss also met the specifications for abnormality according to the Mosenthal and Barry recommendations. However, the fasting, thirty-minute, and sixty-minute values for the group with bone loss were within the presently regarded normal range of blood glucose. There is no question but that it is hazardous to attach a great deal of significance to small changes in alveolar bone loss. Though it is difficult to state exactly how important this particular roentgenographic sign (alveolar bone loss) is, it seems logical that alveolar bone loss cannot be accepted as a sign of good health.

The observations derived from a consideration of the combination of periodontal widening and alveolar bone loss are also enlightening. It is clear from Fig. 6 and Table II that the patients with periodontal widening and alveolar bone loss and those with no periodontal widening and no alveolar bone loss are significantly different with respect to the fasting, one-hour, and two-hour measurements. Nonetheless, the fasting, thirty-minute, and sixty-minute scores, according to present normality standards, are within accepted limits for good health. Also noteworthy, as previously demonstrated with alveolar bone loss, is the $>$ 100 mg. per cent value at two hours, indicating abnormality according to present standards.

Other Factors.—

Age factor: There are some investigators who claim that blood glucose levels are normally higher in the older age groups. There is no disagreement that diabetes mellitus occurs more commonly in the autumnal years of life.

Finally, it is well established that alveolar bone loss is more prevalent in elderly persons. Therefore, the question is whether or not the relationships that have been discussed in this report are wholly or partially due to the age factor.

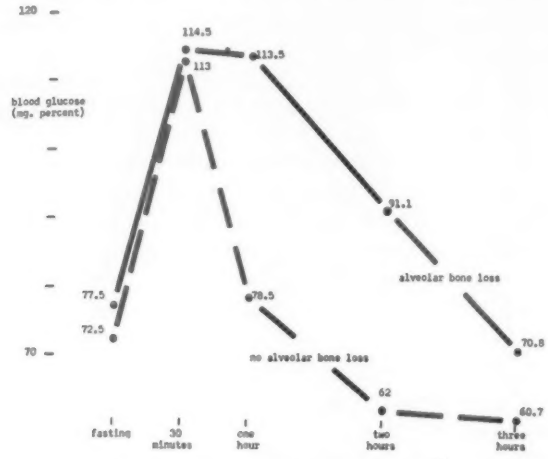


Fig. 7.—Comparison of glucose-tolerance patterns of patients 20 to 29 years of age with and without alveolar bone loss.

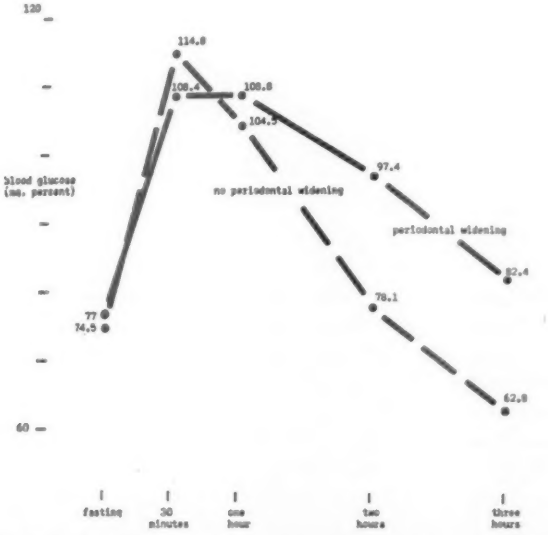


Fig. 8.—Comparison of glucose-tolerance patterns of patients 20 to 29 years of age with and without periodontal widening.

Accordingly, those subjects with and without alveolar bone loss were restudied. Only those subjects between the ages of 20 and 29 years were studied, however,

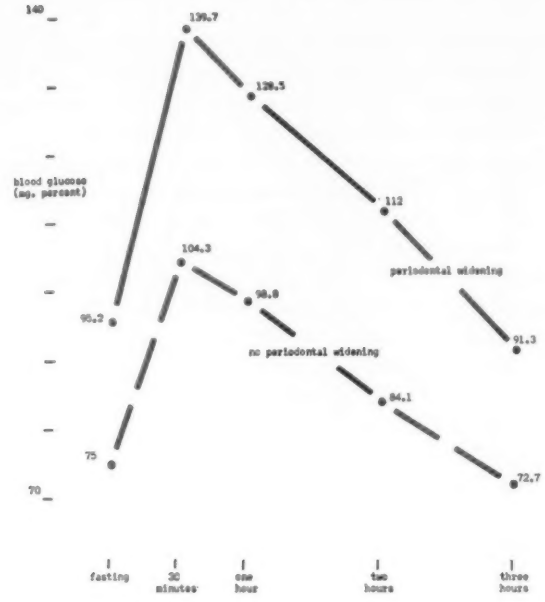
in order that the age factor might be eliminated. Fig. 7 shows the glucose-tolerance patterns for those with and without alveolar bone loss in this one age category. It is clear from Fig. 7 that the two groups are clearly defined. A comparison of Figs. 7 and 5 shows that the differences at some points are less and that at other temporal points they are more. Finally, a comparison of Tables II and III demonstrates that significant differences were present in both instances at both the one-hour and two-hour determinations. It is true that the probability values for the restricted age group are slightly less, over-all, than for the entire group. Thus, it is possible that the glucose and alveolar bone loss relationships may in part be related to age factors.

It should be recalled that in an over-all analysis of the entire group no significant differences were observed in patients with and without periodontal widening. In order to learn whether the age factor might contribute to this lack of relationship, the patients in the 20- to 29-year age group were studied (Fig. 8). It is clear that the glucose-tolerance patterns are different for the two groups. However, the individual curves are not as clearly delineated as for the entire group (Fig. 4). Notwithstanding this fact, it is interesting to observe in Table III that there is a significant difference at the three-hour

TABLE III. STATISTICAL COMPARISON OF MEAN DIFFERENCES

		BLOOD GLUCOSE DIFFERENCES				
		FASTING	30 MINUTES	1 HOUR	2 HOURS	3 HOURS
Alveolar bone loss versus no alveolar bone loss (20- to 29-year age group)	Mean difference	5.000	1.500	35.000	29.100	10.100
	P	> .100	.500	< .025	< .001	> .200
Periodontal widening versus no periodontal widening (20- to 29-year group)	Mean difference	2.500	6.400	4.300	19.300	19.600
	P	> .200	.500	.500	> .200	< .050
Periodontal widening versus no periodontal widening (30- to 39-year group)	Mean difference	20.200	35.400	29.700	27.900	18.600
	P	> .100	> .050	> .200	> .400	> .400
Periodontal widening versus no periodontal widening (40- to 49-year age group)	Mean difference	11.800	36.100	38.700	38.400	21.500
	P	> .200	> .050	> .100	> .100	> .200
Periodontal widening and alveolar bone loss versus no periodontal widening and no alveolar bone loss (patients with 22 to 30 teeth)	Mean difference	17.100	17.300	33.000	46.500	26.600
	P	< .025	> .100	> .050	< .010	> .050
Periodontal widening and alveolar bone loss versus no periodontal widening and no alveolar bone loss (patients without calculus)	Mean difference	3.700	1.400	17.500	36.800	3.700
	P	> .400	.500	> .200	< .050	.500
Periodontal widening and alveolar bone loss versus no periodontal widening and no alveolar bone loss (patients with calculus)	Mean difference	15.400	24.000	46.600	40.500	23.500
	P	< .010	> .050	< .010	< .005	< .005

Fig. 9.



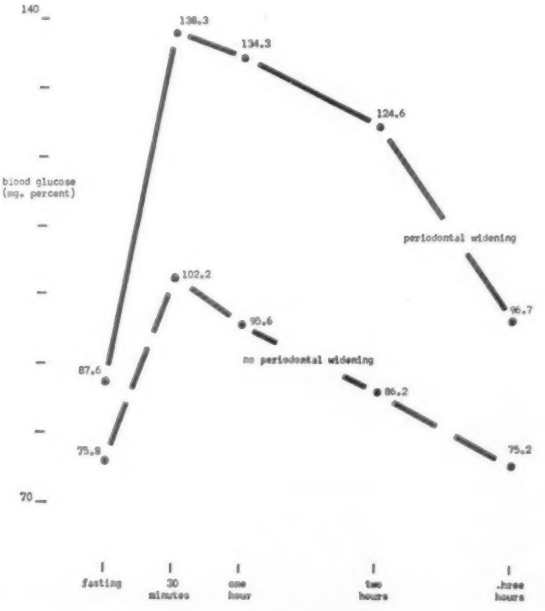


Fig. 10.

Fig. 9.—Comparison of glucose-tolerance patterns of patients 30 to 39 years of age with and without periodontal widening.

Fig. 10.—Comparison of glucose-tolerance patterns of patients 40 to 49 years of age with and without periodontal widening.

point ($p < .050$), whereas no significant differences were observed in an analysis of the entire group (Table II).

Figs. 9 and 10 summarize the relationship of periodontal widening and no periodontal widening in the 30- to 39-year age group and the 40- to 49-year age group. As can be observed from Table III, none of the scores is significant. This probably can be interpreted to mean that in the earlier age groups a relationship does exist between carbohydrate metabolism and this particular roentgenographic finding. In the later age groups, however, other factors apparently become more dominant.

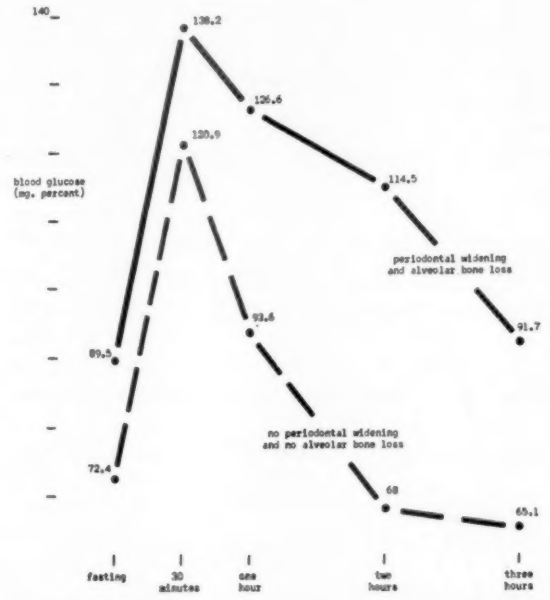
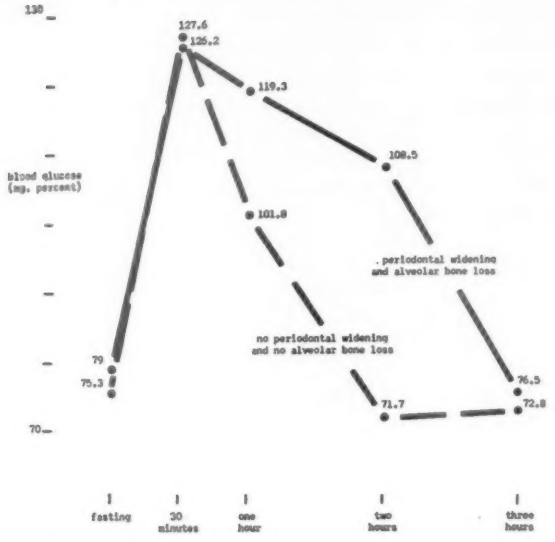


Fig. 11.—Comparison of glucose-tolerance patterns of patients with twenty-two to thirty teeth, with and without periodontal widening and alveolar bone loss.

Number of teeth: The statement is made that roentgenographic findings, such as periodontal widening and alveolar bone loss, may be a function of the number of teeth. Accordingly, the data in this study were rearranged so that the number of teeth could be held constant. Fig. 11 shows the glucose-tolerance patterns for persons, with and without periodontal widening and alveolar bone loss, who have twenty-two to thirty teeth. It is clear from Table III that these two groups of patients differ significantly at the fasting and two-hour determinations. A comparison of Tables II and III shows a decrease in significance when the factor of number of teeth is kept constant. It would seem, therefore, that the number of teeth is a factor in the relationship to periodontal widening and alveolar bone loss. It certainly is not the only factor, however, and it is not dominant enough to destroy the correlation of carbohydrate metabolism and these two roentgenographic findings.

Fig. 12.



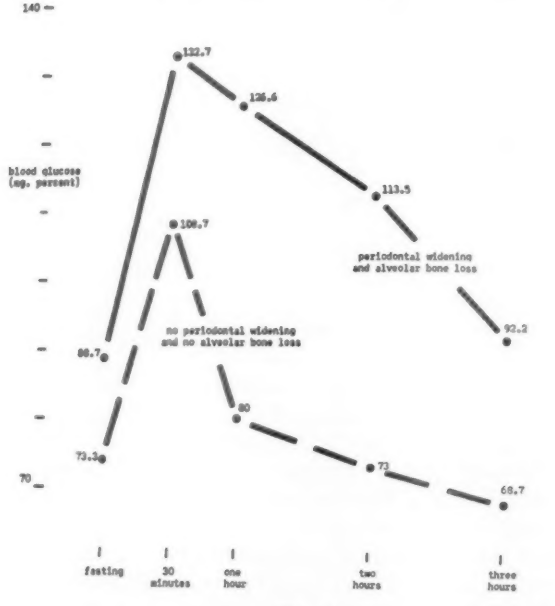


Fig. 13.

Fig. 12.—Comparison of glucose-tolerance patterns of patients with no calculus, with and without periodontal widening and alveolar bone loss.

Fig. 13.—Comparison of glucose-tolerance patterns of patients with calculus, with and without periodontal widening and alveolar bone loss.

Calculus: Mention is often made in the literature that calculus affects alveolar bone loss and periodontal widening. Accordingly, this factor was studied. Figs. 12 and 13 show the glucose-tolerance patterns of patients with and without periodontal widening and alveolar bone loss with the calculus factor kept constant. It is noteworthy, as shown in Table III, that in those patients without calculus the glucose-tolerance patterns were significantly different at the two-hour period as judged by a $p < .05$. Also interesting is the observation (Fig. 12) that the two-hour mean blood glucose shows abnormality as judged by the usual standards. Table III also shows that, when calculus is kept constant, there are significant differences in patients with and without periodontal widening and alveolar bone loss in the fasting, one-hour, two-hour, and three-hour measurements. From the graphs, it would appear that calculus is related to these two roentgenographic findings. However, it does not appear to be the only factor. *As a matter of fact, the grouping of calculus with periodontal widening and alveolar bone loss seems to be the combination in this report which best sets apart the two groups on the basis of glucose-tolerance patterns.*

SUMMARY

1. On the basis of the over-all glucose-tolerance pattern, 100 routine dental patients appear normal if judged by the standards for glucose established by Mosenthal and Barry.

2. From an analysis of the mean two-hour determination of the glucose-tolerance pattern, 100 routine dental patients would be regarded as systemically abnormal.

3. Alveolar bone loss in contrast to periodontal widening appears to be more related to diabetes mellitus.

4. The combination of periodontal widening and alveolar bone loss seems to be more representative of the diabetic patient than independent analysis of these two roentgenographic findings.

5. Within the limits of this study, the evidence suggests that the age factor does play a role in the relationship between alveolar bone loss and glucose metabolism. In the 20- to 29-year age group, the relationship of alveolar bone loss to carbohydrate metabolism is essentially the same as that observed for the entire group. It would have been desirable to study this relationship in older age groups also, but the samples did not permit statistical analysis.

6. Under the conditions of this study, the evidence suggests that the age factor seems to play a role in the relationship of periodontal widening to carbohydrate metabolism. In the 20- to 29-year-old patients, the groups with and without periodontal widening were statistically different at the three-hour measurement. In contrast, for the entire group there was no statistically significant difference. A further analysis of older age groups, however, shows a loss of statistical significance. This can be interpreted to mean that, with age, other factors enter the picture which cancel out the relationship between periodontal widening and carbohydrate metabolism.

7. The literature suggests that the number of teeth is an etiological factor in the development of periodontal widening and alveolar bone loss. We studied the relationship between these two roentgenographic findings, keeping the number of teeth constant. The evidence suggests that the group with periodontal widening and alveolar bone loss was significantly different from the group with no periodontal widening and no alveolar bone loss at the fasting and two-hour determinations. In other words, the statistical significance of the relationship of these two groups decreased when the number of teeth was kept constant. This can be interpreted to mean that the number of teeth operates in the relationship with these roentgenographic findings. However, the number of teeth is not the only factor. More important, it is not significant enough to destroy the correlation between periodontal widening and alveolar bone loss with carbohydrate metabolism.

8. The literature suggests that calculus may play a role in the development of periodontal widening and alveolar bone loss. Accordingly, the patients were divided into two groups, with and without periodontal widening and alveolar bone loss, and at the same time the calculus factor was kept either absent or present. The evidence suggests that in the group without calculus the glucose-tolerance patterns of those with periodontal widening and alveolar bone loss were statistically distinct when compared with the glucose-tolerance patterns of the group in which those two roentgenographic findings were not seen at the two-hour determination. On the other hand, a similar analysis of the patients with calculus showed statistically significant differences between the groups at fasting, one hour, two hours, and three hours. These findings indicate that calculus is a factor in the relationship with periodontal widening and alveolar bone loss. It is not the only one, however, nor is it dominant enough in itself to destroy the correlation observed between these roentgenographic findings and glucose metabolism.

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ROENTGENO-QUESTIONS

How may the shadow of the zygomatic process of the maxilla, which often casts a shadow over the roots of the upper molars, be eliminated from x-ray projections of the upper molar regions?

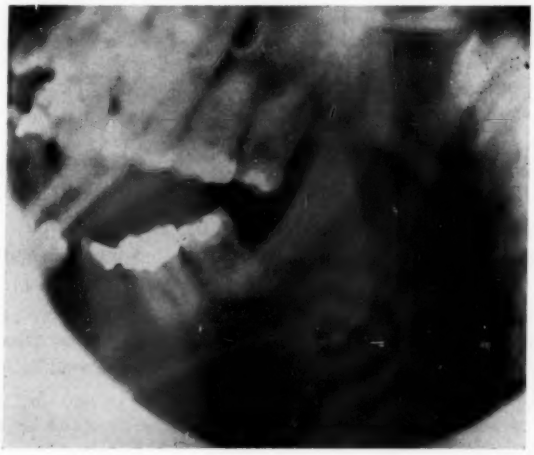
Generally, the shadow of the zygomatic process of the maxilla can be controlled. It can be projected above the film or obliquely anterior or posterior to the area of interest. It is seldom necessary to use greater than a plus 20 degree angulation for upper molar films. This, of course, may not be true for unerupted third molars. By changing the horizontal angulation of the tube, the shadow of the zygomatic process can be thrown posterior to the first and second molars. When the third molar area is studied, it can be projected to the anterior portion of the film. This is particularly necessary in patients who have prominent low zygomatic bones. When the patient has high zygomatic bones, it is usually possible to make the projection under the zygomatic process and not have it appear on the film. Efforts to parallel the tooth and the film through the use of a cotton roll interposed between the lower edge of the film and the palatal surface of the tooth are helpful.

The American Academy of Oral Roentgenology solicits from the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY any questions which deal with technical or interpretive aspects of oral roentgenology. These questions should be sent directly to the editor of this section, Dr. Arthur H. Wuehrmann, School of Dentistry, University of Alabama Medical Center, Birmingham, Alabama; the editor will distribute them for reply to a suitable group within the Academy. Questions, with the answers, will be published at as early a date as possible in "Roentgeno-Questions." Questions, especially those of an interpretive nature, should ordinarily be accompanied by good-quality roentgenograms and a pertinent history. The names of the questioner and the respondent will not be published.

ROENTGENO-ODDITIES

Bilateral Mandibular Canal Enlargement

The accompanying preoperative roentgenogram demonstrates the enlargement (which is bilateral) of the mandibular canal in a patient to be treated by an oblique osteotomy in the ascending ramus for correction of false prognathism. There are no subjective symptoms.



Kurt H. Thoma
Boston, Massachusetts.

Each month this section will bring to the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY one or more roentgenograms which demonstrate unusual, unexpected, rare, or bizarre roentgenographic changes. These roentgenograms will be accompanied by an explanation or by words of inquiry regarding the particular change. All films used in this section will be accepted with the understanding that 2 by 2 or 3¼ by 4 inch slides or glossy photographs of the films will be made available to interested readers through the editor of the American Academy of Oral Roentgenology at the individual's expense. The cost will involve only the photographer's charges. Each slide or print will give credit to the donor. Interesting roentgenograms are solicited from all sources. Please be certain to identify your films properly so that they can be returned. All material for publication should be submitted to Dr. Arthur H. Wuehrmann, University of Alabama School of Dentistry, Medical Center, Birmingham, Alabama.

ORAL PATHOLOGY

THE RELATIONSHIP OF ORAL CANCER TO GENERALIZED CONNECTIVE TISSUE CHANGES

A Review of Forty Postmortem Examinations

James F. Smith, B.S., D.D.S., Ph.D., Memphis, Tenn.*

THE importance of generalized tissue changes in the cancer patient has long been recognized. Cachexia, weight loss, and blood changes are commonly seen and may be the result of altered tissue response.[1] In the past, important generalized tissue changes may have been overshadowed by our concentration on neoplastic changes only.

Evidence has been offered that liver changes, such as cirrhosis, and carcinoma of the tongue often occur in the same patient.[2]

The purpose of this article is to present findings concerning the postmortem examination of twenty patients who had oral cancer (Table I). The type of tumor and its location in the oral cavity are stated in each case. The oral lesions had been biopsied. The patients were treated in the West Tennessee Cancer Clinic, and their postmortem examinations were performed at the University of Tennessee Institute of Pathology.

The cause of death was determined in each case, and the tissues and organs were examined for connective tissue changes.[3]

For comparison, we chose twenty other cases in which the age, sex, and cause of death were identical, the only exception being that this group did not have oral cancer; the noncancer group is not discussed in detail (Table II).

A brief discussion of the individual oral cancer cases follows.

CASE 1.—The patient was an 83-year-old man with epidermoid carcinoma of the right buccal mucosa. There were moderate focal areas of degeneration in the liver, with atrophy and necrosis. There was minimal fibrosis, as well as marked generalized arteriosclerosis. Moderate myocardial fibrosis was observed. Adenocarcinoma of the prostate was found at autopsy.

CASE 2.—This patient, an 80-year-old woman with epidermoid carcinoma of the tongue and floor of the mouth, had a long-standing history of rheumatoid arthritis. The liver showed marked fatty change but no fibrotic changes. There was generalized arteriosclerosis.

*Assistant Professor of Oral Medicine, University of Tennessee Dental School; Special Fellow, United States Public Health Service.

CASE 3. The patient, a 64-year-old woman with epidermoid carcinoma of the tongue, had atrophy and brown pigmentation of the liver, but there was little evidence of fibrosis. There was generalized marked arteriosclerosis and minimal myocardial fibrosis.

CASE 4.—A 70-year-old woman with epidermoid carcinoma of the tongue had marked congestion of the liver but no fibrosis. There was generalized arteriosclerosis, as well as minimal fibrosis of the pancreas.

CASE 5.—The patient, a 61-year-old man with epidermoid carcinoma of the alveolar ridge and floor of the mouth had marked congestion and an inflammatory process of the liver, but little fibrosis. There was marked arteriosclerosis and calcification in the coronary vessels and aorta, as well as nodular hyperplasia of the prostate.

CASE 6.—This was the case of a 72-year-old man with epidermoid carcinoma of the tongue. There was chronic, passive congestion of the liver, with little evidence of fibrosis. There also was marked arteriosclerosis throughout the circulatory system, as well as marked arteriolar nephrosclerosis.

CASE 7.—The patient was a 47-year-old man with epidermoid carcinoma of the floor of the mouth. There was minimal fibrosis of the liver, as well as moderate generalized arteriosclerosis of all major vessels. There was also moderate myocardial fibrosis.

CASE 8.—A 72-year-old man with adenocarcinoma of the hard palate had moderate scarring and fibrosis of the liver and marked prostatic fibrosis and hypertrophy. The cardiovascular system showed generalized arteriosclerosis and moderate myocardial fibrosis. Cause of death in this patient was adenocarcinoma of the jejunum, with widespread metastases.

CASE 9.—The patient in this case was a 70-year-old woman with malignant epidermoid carcinoma of the alveolar ridge. There was minimal fibrosis of the liver, as well as generalized arteriosclerosis.

CASE 10.—The patient, a 63-year-old man with epidermoid carcinoma of the tongue, had moderate fibrosis in the lungs and liver; there was severe atherosclerosis of the aorta.

CASE 11.—A 66-year-old woman presented an epidermoid carcinoma of the tongue. There was minimal fibrosis of the liver, as well as moderate myocardial fibrosis. There also was generalized arteriosclerosis.

CASE 12.—The patient was a 43-year-old man with epidermoid carcinoma of the buccal mucosa. He had moderate myocardial fibrosis and no fibrosis of the liver.

CASE 13.—The liver of this 85-year-old man with epidermoid carcinoma of the tongue showed fatty infiltration and brown pigmentation but very little fibrosis. There was moderate myocardial fibrosis and generalized arteriosclerosis. There was also prostatic hyperplasia.

CASE 14.—A 54-year-old man with carcinoma of the floor of the mouth and tongue had little fibrosis but extensive fatty infiltration of the liver. There was marked fibrosis of the spleen, hyperplasia of the prostate, and generalized arteriosclerosis.

CASE 15.—The patient, a 51-year-old woman with epidermoid carcinoma of the tongue, had marked cirrhosis of the liver. There was marked myocardial fibrosis and moderate arteriosclerosis.

CASE 16.—A 66-year-old man with epidermoid carcinoma of the tongue had marked fibrosis of the pancreas and prostate, as well as marked myocardial fibrosis. There was very little fibrosis of the liver.

CASE 17.—The patient, a 76-year-old woman with epidermoid carcinoma of the hard palate, had no fibrosis of the liver. However, there was severe arteriosclerotic change throughout the major vessels. The cause of death was adenocarcinoma of the colon.

TABLE I. POSTMORTEM EXAMINATIONS OF ORAL CANCER PATIENTS

CASE NO.	TYPE OF TUMOR	LIVER	PANCREAS	SPLEEN	MYOCARDIUM	CARDIOVASCULAR SYSTEM	PROSTATE
1	Buccal mucosa epidermoid carcinoma	Necrosis and atrophy; minimal fibrosis	No change	No change	Moderate fibrosis	Moderate generalized arteriosclerosis	Adenocarcinoma
2	Epidermoid carcinoma of tongue	Fatty infiltration; no fibrosis	No change	No change	No change	Marked generalized arteriosclerosis	
3	Epidermoid carcinoma of tongue	Atrophy; brown pigmentation; minimal fibrosis	No change	No change	Minimal fibrosis	Marked generalized arteriosclerosis	
4	Epidermoid carcinoma of tongue	Marked congestion; no fibrosis	Minimal fibrosis	No change	No change	Moderate generalized arteriosclerosis	
5	Epidermoid carcinoma of floor of mouth and alveolar ridge	Marked congestion; minimal fibrosis	No change	No change	No change	Marked generalized arteriosclerosis	Nodular hyperplasia
6	Epidermoid carcinoma of tongue	Chronic passive congestion	No change	No change	No change	Moderate arteriolar nephrosclerosis	
7	Epidermoid carcinoma of floor of mouth	Minimal fibrosis	No change	No change	Moderate fibrosis	Moderate generalized arteriosclerosis	
8	Adenocarcinoma of hard palate	Moderate scarring and fibrosis	No change	No change	Moderate fibrosis	Generalized arteriosclerosis	Marked fibrosis
9	Epidermoid carcinoma of alveolar ridge	Minimal fibrosis	No change	No change	No change	Generalized arteriosclerosis	
10	Epidermoid carcinoma of tongue	Moderate fibrosis	No change	No change	No change	Severe generalized arteriosclerosis	
11	Epidermoid carcinoma of tongue	Minimal fibrosis	No change	No change	Moderate fibrosis	Moderate generalized arteriosclerosis	
12	Epidermoid carcinoma of buccal mucosa	No change	No change	No change	Moderate fibrosis	No change	No change
13	Epidermoid carcinoma of tongue	Fatty infiltration; no fibrosis	No change	No change	Moderate fibrosis	Moderate generalized arteriosclerosis	Hyperplasia

14	Epidermoid carcinoma of tongue and floor of mouth	Fatty infiltration	No change	Marked fibrosis	No change	Minimal generalized arteriosclerosis	Hyperplasia
15	Epidermoid carcinoma of tongue	Marked cirrhosis	No change	No change	Marked fibrosis	Moderate generalized arteriosclerosis	
16	Epidermoid carcinoma of tongue	No change	Marked fibrosis	No change	Marked fibrosis	No change	Marked fibrosis
17	Epidermoid carcinoma of hard palate	No change	No change	No change	No change	Marked generalized arteriosclerosis	
18	Epidermoid carcinoma of alveolar ridge	Moderate fibrosis	No change	No change	No change	Marked generalized arteriosclerosis	Fibrosis and adenocarcinoma
19	Epidermoid carcinoma of alveolar ridge	No change	No change	No change	No change	Moderate generalized arteriosclerosis	Fibrosis
20	Epidermoid carcinoma of tongue and floor of mouth	Congestion; focal necrosis	No change	No change	No change	Minimal generalized arteriosclerosis	

TABLE II. COMPARATIVE POSTMORTEM EXAMINATIONS OF NONCANCER PATIENTS

CASE NO.	LIVER	PANCREAS	SPLEEN	MYOCARDIUM	CARDIOVASCULAR SYSTEM	PROSTATE
1	Minimal fibrosis	No change	Minimal fibrosis	No change	Arteriosclerosis, moderate	Hyperplasia
2	Cirrhosis	Moderate fibrosis	No change	Moderate fibrosis	Arteriosclerosis, marked	
3	No change	No change	Moderate fibrosis	No change	Arteriosclerosis, marked	
4	Congestion	No change	No change	Minimal fibrosis	Arteriosclerosis, moderate	
5	Moderate fibrosis	No change	Moderate fibrosis	No change	Arteriosclerosis, moderate	Hyperplasia
6	Moderate fibrosis	Moderate fibrosis	No change	No change	Arteriosclerosis, moderate	
7	Moderate fibrosis	No change	No change	Minimal fibrosis	No change	
8	No change	No change	No change	Minimal fibrosis	Arteriosclerosis, moderate	Marked hypertrophy
9	No change	Moderate fibrosis	No change	No change	No change	
10	Moderate fibrosis	No change	No change	No change	Arteriosclerosis, moderate	
11	Minimal fibrosis	Minimal fibrosis	No change	No change	Arteriosclerosis, moderate	
12	Cirrhosis	No change	Minimal fibrosis	Minimal fibrosis	Arteriosclerosis, moderate	Hyperplasia
13	No change	No change	Minimal fibrosis	No change	Arteriosclerosis, moderate	Benign hypertrophy
14	Minimal fibrosis	No change	Minimal fibrosis	No change	Arteriosclerosis, minimal	No change
15	Moderate fibrosis	Moderate fibrosis	No change	No change	Arteriosclerosis, moderate	
16	No change	Minimal fibrosis	No change	No change	Arteriosclerosis, minimal	Hyperplasia
17	Moderate fibrosis	No change	No change	Minimal fibrosis	Arteriosclerosis, moderate	
18	Marked cirrhosis	No change	Minimal fibrosis	Minimal fibrosis	Arteriosclerosis, marked	Benign hypertrophy
19	Minimal fibrosis	No change	No change	No change	Arteriosclerosis, minimal	Minimal fibrosis
20	Marked congestion	No change	No change	Moderate fibrosis	Arteriosclerosis, moderate	

CASE 18.—A 67-year-old man with epidermoid carcinoma of the maxillary alveolar ridge had focal areas of fibrosis of the liver. There was fibrosis and carcinoma of the prostate.

CASE 19.—The patient, a 31-year-old man with epidermoid carcinoma of the mandibular alveolar ridge had no fibrotic changes in the liver. However, there was fibrosis of the prostate and moderate generalized arteriosclerosis.

CASE 20.—The patient was a 38-year-old woman with epidermoid carcinoma of the floor of the mouth and tongue. There was generalized congestion and focal necrosis in the liver, but no fibrosis. There was minimal arteriosclerosis throughout the major vessels.

SUMMARY

Twenty postmortem examinations of patients who had oral cancer were reviewed. The presence of connective tissue changes in various organs was noted and recorded to determine whether the tissue changes were consistent in these cases. The results were then compared with the corresponding noncarcinoma cases.

CONCLUSION

A thorough study of postmortem findings in twenty cases of oral cancer, which included ten cases of epidermoid carcinoma of the tongue, revealed that all cases included one or more connective tissue changes in specific organs. This, however, is not considered significant, since a review of many cases in patients of the same ages without oral cancer showed just as many generalized connective tissue changes in the various organs.

It is our opinion, therefore, that cirrhosis of the liver and other connective tissue changes do not occur with any greater frequency in patients with carcinoma of the tongue and oral cavity than in patients of comparable age, sex, and race who do not have carcinoma.

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KERATOACANTHOMA OF THE ORAL CAVITY

Report of a Case

R. W. Helsham, D.D.Sc., F.D.S.R.C.S., and G. Buchanan, B.D.S.,
Sydney, Australia

KERATOACANTHOMA is a moderately common lesion of the skin, although its differential diagnosis is of recent origin. It has been reported under various names, such as self-healing epithelioma, molluscum sebaceum, molluscum pseudocarcinomatosium, verrugoma, and pseudoepitheliomatous hyperplasia. The lesions may occur anywhere on the skin. A review of the literature, however, has not disclosed any report of an oral lesion. According to Musso,[1] "They occur on the face, neck, backs of the hands, wrists and arms. There would seem to be no reason why this lesion should not occur on any part of the body."

Prior to 1950, when Rook and Whimster[2] published a definite account of the histology and natural history of the lesion, these tumors were generally diagnosed as squamous-cell carcinomas, although cases had been recorded as early as 1929. Even though keratoacanthomas exhibit the clinical appearance of a squamous-cell carcinoma, they are benign in character. There are reports of lymphadenitis in the proximity of these lesions which has been proved to be due to associated inflammation, but in no case has there been evidence of invasive tendencies.

CLINICAL SIGNS

Beare[3] states that lesions of the skin pursue a definite clinical course. Growth of the lesion takes place rapidly over a period of approximately eight to twelve weeks, following which there is cessation of growth for a varying period. Subsequently, there may be spontaneous resolution if the lesion has not already been treated. The maximum size of the tumor is usually 1 to 1.5 cm. in diameter. Grinspan and Abulafia[4] describe three distinct clinical entities with some difference in the histologic picture. The first type described is the verrugoma, in which the lesion is wartlike with a papillomatous central zone covered with a scale which is difficult to detach. The second type is the molluscum sebaceum, which is an elevated nodule with a crateriform central

From the United Dental Hospital of Sydney.

opening filled with horny material. The third is the nodulovegetating type, which is a raised mushroomlike growth with surface lobulations, separated by furrows, giving the appearance of a papillomatous vegetating lesion. The appearances described have also been seen in some carcinomas. All types described are freely movable on the deeper tissues. The lesions themselves are resilient and may be painful on pressure. Occasionally, there may be a slightly painful satellite adenitis. Although there is no definite etiology, some cases of verrugoma and molluscum sebaceum and all cases of the nodulovegetating types give a history of prior trauma.

HISTOLOGY

Beare[3] states that the bulk of the tumor is made up of long, coiled papilliferous processes, all producing large quantities of well-formed keratin. The basement membrane is often missing in places, owing to the rapid growth and the associated reactive inflammatory change. The lesion does not invade. Whittle and Lyell[5] give the following description: "The histological features suggest squamous carcinoma—but they are not anaplastic and the growing epithelial cords do not transgress the dermal boundary." Grinspan and Abulafia[4] make slight differentiation between the three clinical types described, with the exception that all types have thin epithelial cords infiltrating the dermal connective tissue and there is no atypia of cells.

Verrugoma.—The changes are primarily in the epidermis where the prickle layer shows marked hypercanthosis. Inflammation is not pronounced.

Molluscum Sebaceum.—The base of the lesion shows irregular acanthosis and pseudoepitheliomatous hyperplasia with small follicular keratinous cysts with cornified centers.

Nodulovegetating Type.—The over-all picture is that of heavier hyperkeratic follicles infiltrating the corium. There is a dense invasion of general inflammatory cells, and some micro-abscesses may be seen at the depth of the horny pearls.

TREATMENT AND PROGNOSIS

Skin lesions have been treated by various means. Prior to 1929 they were treated as squamous-cell carcinomas. Since the establishment of a differential diagnosis, best results have been obtained by curettage and cauterization of the base. However, cures have been reported following radiation, biopsy, administration of antibiotics and antisyphilitic drugs, application of carbon dioxide snow, and complete excision. All authors stress that spontaneous resolution can take place, although in these cases there is usually scar formation which can be avoided by more definite treatment. It must be emphasized that, despite the benign nature of the lesion, biopsy must be performed. Clinical distinction from squamous-cell carcinoma is not always possible. All cases reported as keratoacanthoma have responded to simple treatment with no recurrence, which again emphasizes their benign character.

CASE REPORT

A 38-year-old man of Hungarian birth was referred to this hospital by his physician for treatment of an oral ulceration. The patient stated that he sought dental attention a number of years ago in Russia. The upper right canine tooth had been given root therapy, and a full metal crown has been constructed.

For three weeks prior to his attendance at this hospital, the patient had noticed soreness and ulceration on the gingival margin over the tooth. He further stated that he was employed in the electroplating section of an automobile factory, where his work necessitated the wearing of leather gloves as protection against acid. He remembered that the area above the upper right canine tooth had felt sore and that he had touched it several times at work with acid-contaminated gloves. Later he noticed the ulceration. During the week before, the lesion had greatly increased in size. The patient had applied iodine of unknown strength to the lesion four or five times daily for approximately five days. He also stated that he had, at times, noticed small skin eruptions on the lower parts of his arms above the area covered by his gloves.

Fig. 1.—Photograph taken when patient was first seen. Note the lesion over the upper right canine.

Oral examination revealed a fungating tumor, approximately 20 mm. in diameter, situated on the buccal mucous membrane of the maxilla in the upper right canine region (Fig. 1). The lesion extended around the mesial aspect of the canine tooth and had involved some palatal mucous membrane. The lesion was raised approximately 8 mm. above the level of the surrounding tissue and was enclosed by a cuff of apparently normal mucous membrane. The surface was irregularly nodular and predominantly white in color. On palpation the lesion bled easily; it was fairly soft and not movable.

Diagnosis.—Roentgenograms of the region did not disclose any abnormality other than an even alveolar resorption consistent with the patient's age. Smears and scrapings from the surface of the lesion were obtained, and bacteriologic examination was carried out. No pathogenic organisms were identified. Routine laboratory tests were performed. Hematologic examination revealed a lowered hemoglobin value, with other indications of slight anemia. White cells were normal. Blood chemistry and urinalysis were within normal limits; serologic tests and a lung-field survey were negative.

During the week that laboratory tests were being made, the size of the lesion increased, with extension to the palatal mucosa, despite the local application of astringents. A provisional diagnosis of squamous-cell carcinoma was made, and it was decided that a biopsy of the lesion should be performed.

Accordingly, the patient was premedicated and the area was anesthetized by local infiltration well away from the margins of the lesion. A wedge-shaped piece of tissue was excised, extending from apparently normal mucosa to the center of the lesion.

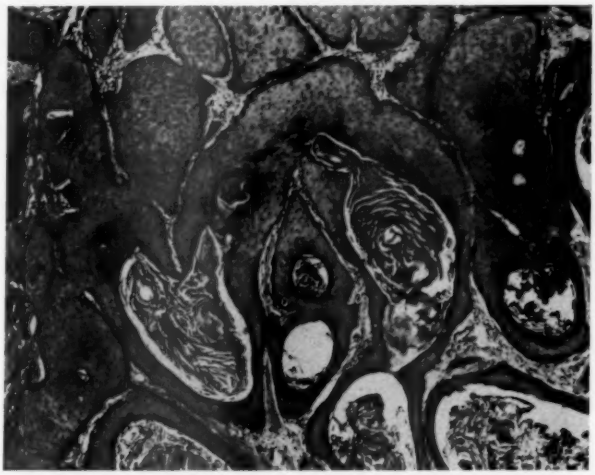

Fig. 2.—A section of the tumor showing epithelical lobules containing keratin.

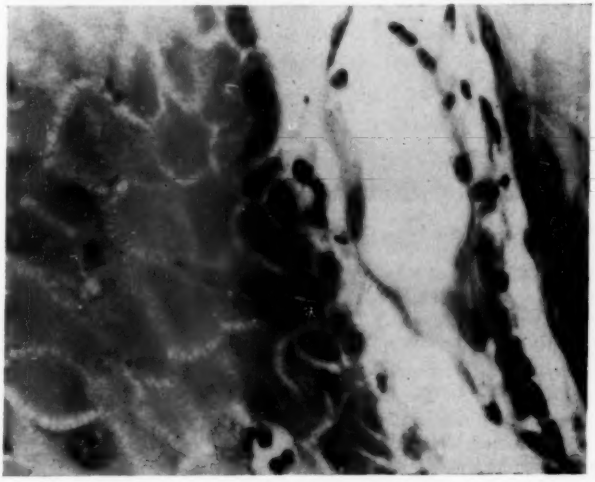

Fig. 3.—High-power photomicrograph showing the margin of a lobule and interlobular connective tissue.

Hemorrhage, which was quite marked, was controlled by pressure followed by the insertion of an absorbable hemostatic into the wound. The biopsy specimen was submitted for examination by a pathologist who reported that the appearance strongly suggested an early carcinoma but requested a larger specimen before making a definite diagnosis.

Subsequently, a further biopsy specimen was taken and the following report was received from the pathologist: "The lesion shows a most unusual pseudoepitheliomatous hyperplasia which resembles squamous carcinoma but cannot be labelled malignant at present. Its picture is that of a keratoacanthoma (self-healing epithelioma) and had it been on the skin on the face or hand I would have called it this." (Figs. 2 and 3.)

The histologic appearance of the lesion showed the outer surface as a wide band of free keratin and debris. The surface was irregular. Within the irregular epithelial band were some islands of keratin, and there were downward prolongations of epithelium leading toward lobules separated by connective tissue. A typical lobule consisted of flattened, deeply staining cells on the outside with conspicuous intercellular bridges. Deeper, the cells were normal-appearing epithelial cells. Toward the center of the lobule the cells greatly increased in size, had very deeply staining globules of keratohyalin, and were circularly arranged around keratin. In some lobules this process was only beginning; in others, there were large central keratin "pearls." Separating the lobules was connective tissue, heavily infiltrated in some areas with inflammatory cells. The lesion had not invaded the periosteum.

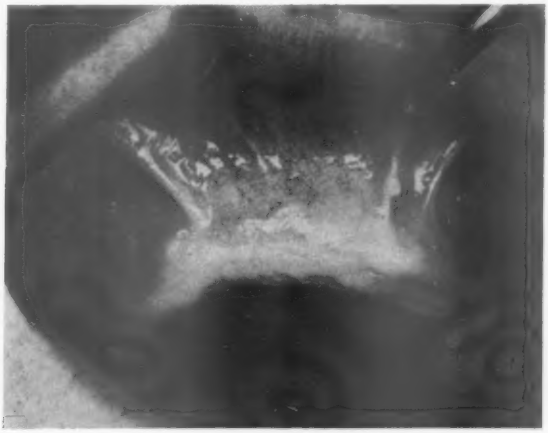

Fig. 4.—Photograph taken eight months after final healing.

At this stage, the patient was seen by the hospital's honorary general surgeon, who requested extraction of the upper right canine tooth. Subsequently under general anesthesia, the lesion was curetted. The pathologic report again confirmed the diagnosis of keratoacanthoma.

Postoperatively, the posterior edge of the ulcer swiftly healed, but the anterior edge continued to extend in the direction of the upper right central incisor. Caustics were applied—copper sulfate solution for three days and a nitric acid stick twice daily for four days. The ulcer healed in response to this treatment. Later, the remaining maxillary teeth were extracted and a full upper denture was constructed. When the patient was last seen eight months after final healing, the maxilla was normal, with no sign of recurrence or deformity (Fig. 4).

COMMENT

The histologic appearance and the ease of healing definitely establish this lesion as a type of keratoacanthoma. According to the classification made by

Grinspan and Abulafia[4] this appears to have been the nodulovegetating type, both from its clinical appearance (Fig. 1) and from its histopathologic structure (Figs. 2 and 3).

Until recently all skin lesions of this type were treated radically as squamous-cell carcinoma. It is interesting to speculate as to whether or not all tumors diagnosed as oral carcinomas in the past were, in fact, malignant.

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TUMORS OF THE SALIVARY GLANDS, WITH A REVIEW OF 150 CASES

James F. Smith, B.S., D.D.S., Ph.D., Memphis, Tenn.*

TUMORS of the salivary glands present numerous problems for the pathologist. These tumors are often difficult to classify, and there have been many classifications by numerous authors. In some cases it is difficult to determine whether a given tumor is benign or malignant.

A benign tumor of the major salivary glands will usually grow to a larger size than does the malignant tumor. The malignant tumor will vary in its cellular and fibrous tissue components, either of which may obliterate the normal tissue and change the consistency of the gland. The malignant tumor becomes fixed to skin and bone and may invade the mandible. The muscles of mastication may be invaded, and the patient will demonstrate trismus. The malignant tumor of the parotid gland may invade and cause ulceration of the skin. The malignant tumors may show variable degrees of lymphatic metastasis. In our survey, we found metastasis in about 20 per cent of the salivary gland tumors that were malignant. Metastasis, which seems to be slow in most cases, has been reported in bone, soft tissue, and lungs.

No attempt will be made to discuss all types of salivary gland tumors, but those found most often in our survey will be discussed briefly.

MALIGNANT TUMORS OF SALIVARY GLAND

The adenoid cystic carcinoma (basaloid mixed tumor, cylindroma, etc.) may have its origin in the major salivary glands or in the accessory salivary glands. This tumor has a slow, persistent growth pattern and recurs frequently. Grossly, the tumor may resemble the mixed tumor; microscopically it is composed of small cells that resemble the basal cells of the epithelium. There are dark-staining nuclei and very little cytoplasm in the basal-like cells. The cells are arranged in cords, or acini. The stroma is usually moderate in amount and may be arranged in cylinders. This tumor is primarily a surgical problem. The prognosis is rather poor unless the tumor is discovered and treated early.

The origin of the epidermoid carcinoma remains a subject of controversy. Some authors express the opinion that this tumor arises from ductal epithelium. Regardless of its origin, it has all the histologic elements, including keratinization, of the squamous-cell carcinoma of other regions.

*Assistant Professor of Oral Medicine, University of Tennessee Dental School; Special Fellow, United States Public Health Service.

The mucoepidermoid tumor, which may be either benign or malignant, may present a difficult diagnostic problem. The mucoepidermoid carcinoma arises from ductal epithelium and contains squamous cells and mucin-producing cells. The greater the amount of mucin, the greater is the probability that the tumor is benign.

Fig. 1.

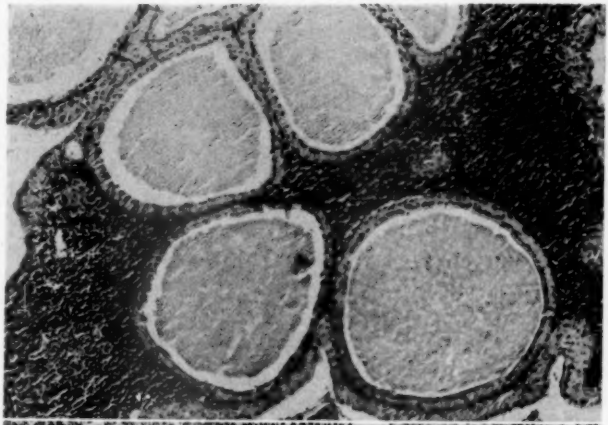
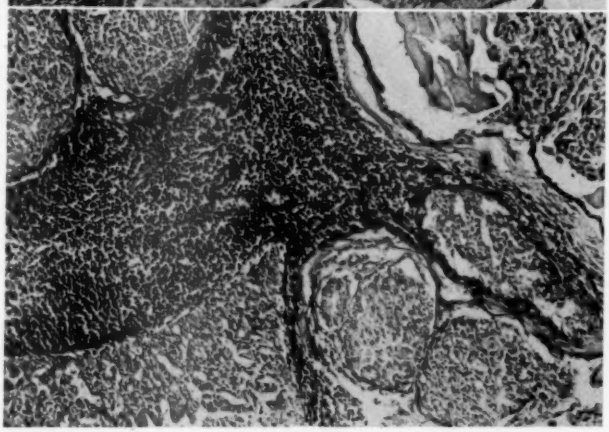


Fig. 2.



Figs. 1 and 2.—Papillary cystadenoma lymphomatosum. Note lymphoid stroma and epithelial parenchyma forming tubules and lining cystic spaces. Two cases.

Malignant transformation can occur in the adenomas, though again the classification is still controversial.

Reticulum-cell sarcoma and lymphosarcoma are found in the salivary glands, and their microscopic appearance is the same as in other reticuloendothelial tissue tumors.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Figs. 3 to 6.—Benign mixed tumors. Note variation in structural components of tumors from four cases.

TABLE I. A STUDY OF SIXTY-TWO MALIGNANT TUMORS OF THE MAJOR SALIVARY GLANDS

Site of tumor	
Parotid gland	56
Submaxillary gland	6
Race	
Caucasian	41
Negro	21
Sex	
Male	37
Female	25
Average age	56 years
Survival rate	
Expired in 5 years or less	28
Lived 5 years or longer	34
Time lapse between chief complaint and treatment	19 months
Treatment	
Surgery	47
X-ray and surgery	15
Metastasis	15
Recurrence	21
Types of tumors	
Malignant mixed tumor	4
Adenocarcinoma	41
Adenoid cystic carcinoma	8
Mucoepidermoid tumor	5
Epidermoid tumor	3
Fibrosarcoma	1

Fibrosarcoma is a rare tumor, but it may occur. In our survey, we found only one case over a period of fifteen years.

BENIGN TUMORS OF THE SALIVARY GLANDS

The mixed tumor of the salivary gland composes, by far, the majority of tumors of this region. At present, opinions vary as to whether this tumor is

TABLE II. A STUDY OF EIGHTY-EIGHT BENIGN TUMORS OF THE MAJOR SALIVARY GLANDS

Site of tumor	
Parotid	79
Submaxillary	9
Race	
Caucasian	51
Negro	37
Sex	
Male	39
Female	49
Average age	51
Survival rate	
Expired in 5 years (all causes)	28
Lived 5 years or longer	60
Time lapse between chief complaint and treatment	27 months
Treatment	
Surgery	74
No treatment	14
Recurrence	16
Types of tumors:	
Mixed-cell tumor	68
Papillary cystadenoma lymphomatosum	4
Adenoma	11
Mucoepidermoid tumor	3
Mikulicz's disease	2

Fig. 7.

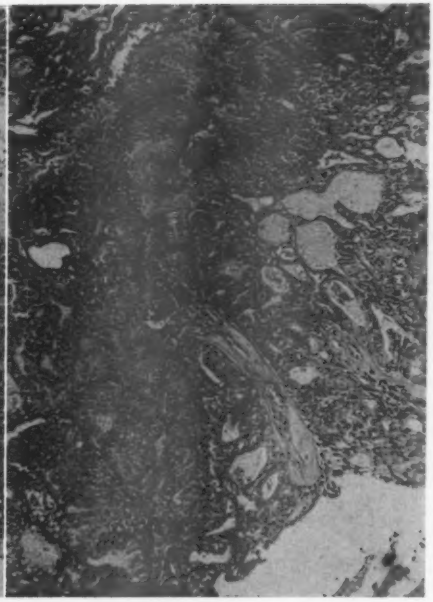


Fig. 8.

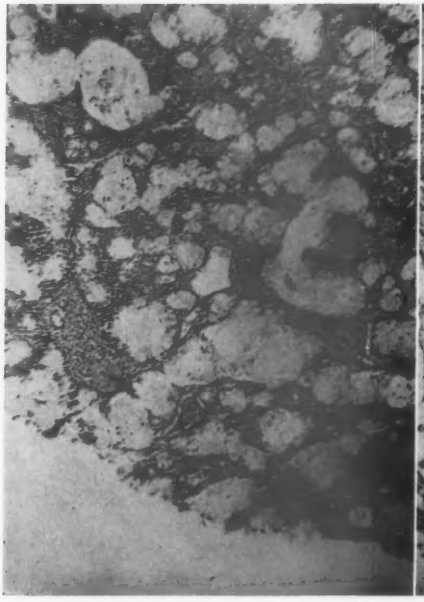


Fig. 9.

Fig. 10.

Figs. 7 to 10.—Mucoepidermoid tumors. Note the variation in mucous gland element and epidermoid cells in the different tumors from four cases.

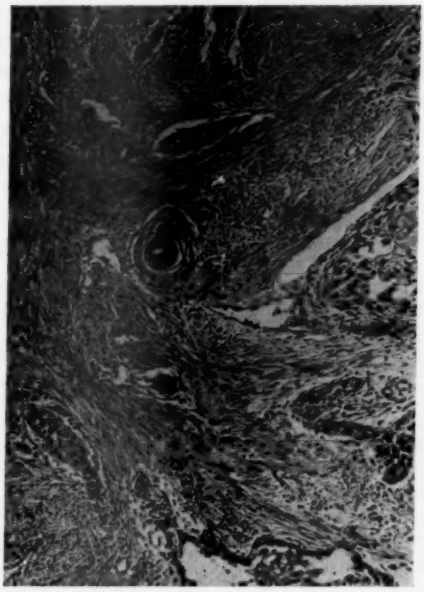


Fig. 11.—Squamous-cell carcinoma of the parotid gland.

Fig. 12.—Fibrosarcoma of the parotid gland.

derived from both epithelial and mesenchymal tissues or simply from ductal cells. There seems to be little to gain from this controversy, since tissues of either type may predominate or be found in equal amounts.

The benign mixed tumor, or pleomorphic adenoma, may be quite large. It is usually freely movable, and it is located most often just superior to the junction of the body and ramus of the mandible at the posterior border. The tumor is usually encapsulated, with the capsule varying in thickness. When there is a predominance of cartilage, the tumor may appear blue-white in color, while those tumors with less cartilage may vary from white to yellow.

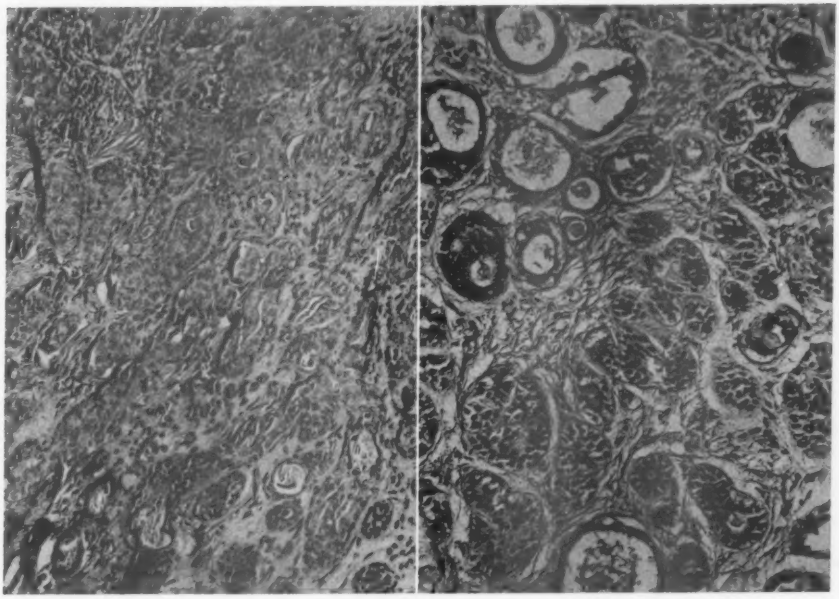


Fig. 13. Fig. 14.

Figs. 13 and 14.—Adenocarcinoma of the parotid gland, demonstrating two histologic pattern types from two cases.

Microscopically, many and varied types of tissue patterns are seen. A great majority of these tumors show strands and islands of cells that may blend into cartilaginous-like tissue or into epithelial-like areas.

The papillary cystadenoma lymphomatosum is made up of lymphoid and epithelial tissue. There are cystic spaces in which the papillary projections with lymphoid matrices can be seen. Eosinophilic columnar cells surround these papillary projections. A homogenous material may be found in the cystic spaces. These tumors are almost always small and well encapsulated.

The adenoma may be predominantly of the mucous or serous type. The oxyphilic adenoma is a rare, small tumor whose large eosin-staining cells may occur in sheets or cords.

Mikulicz's disease is characterized by the replacement of normal glandular tissue by lymphoid tissue, leaving islands or strands of acini.

The mucoepidermoid tumor may be difficult to diagnose as to its being benign or malignant. The benign type does not have the malignant features of the epidermoid component seen in the malignant form; instead, there may be masses or sheets of small, dark-staining round cells.

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ENDODONTICS

The American Association of Endodontists

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THE CONSERVATIVE TREATMENT OF EXTENSIVE AREAS OF PERIAPICAL PATHOLOGY

Max M. Weinreb, D.D.S., M.S., Jerusalem, Israel*

INTRODUCTION

ROOT-END resection has been practiced for a long time as a method of treating infected periapical areas.

The term "root resection" implies the cutting-off of some portion of a root end for the purpose of removing what was presumed to be pathologic tissue associated with the apex. It has been customary to mention, among the indications for resection,[5] (1) extensive destruction of the periapical tissues, bone, or periodontal membrane involving not more than one-third of the root apex, and (2) the presence of a crater-shaped erosion of the root apex indicating destruction of apical cementum. The procedure is contraindicated, however, when (1) general medical or psychological conditions exclude the use of surgery and (2) more than one-third of the apical end of the root is involved.

Lately, however,[2, 11] a radical change in this line of thinking has been brought about by a better understanding of the pathology of the tissues involved. This new concept is based chiefly on the realization that in cases of granuloma or chronic periapical abscess the tissues at the apical end consist mainly of granulation tissue.

Boyle[2] proved that this "granuloma" is not harmful but acts as a defense against the spread of infection. By means of an excellent example, he showed that granulation tissue is not an area in which bacteria live but one in which they are destroyed. The defensive nature of the granulation tissue is further proved by the fact that it disappears after the extraction of an infected tooth or after successful root canal therapy.

Since this granulation tissue is beneficial and attests to a defense mechanism of the body, it is clear that it should be preserved and not removed

*Lecturer in Oral Histology, Department of Anatomy, Schools of Dentistry and Medicine, Hebrew University—Hadassah, Jerusalem, Israel.

surgically. When the original cause has been treated and eliminated, this "defense" tissue will be resorbed, since its presence is no longer needed, and normal anatomic conditions will be re-established around the apex.

In the light of this new realization, we need to re-evaluate the indications for root-end resection and limit this procedure to the very few cases in which anatomic conditions make resection the only method of treatment. Some of our concepts regarding root canal treatment should be expanded to include procedures which will help Nature resorb faster and more completely the barrier that it had put up initially against the advance of infection.

REVIEW OF LITERATURE

The treatment of the periapical tissues is seldom deemed sufficiently important to be considered separately. It was argued by most authors that, since this is only a "reaction" to the infection of the canal, it should be sufficient to sterilize the canals and seal them hermetically. It was thought that when the cause had thus been removed, the reaction would disappear by itself.

Some authors, however, wondered whether, after effective sterilization and sealing of the canal, the periapical tissues still harbor bacteria and hence could represent a source of residual infection. They tried, therefore, to influence and treat these periapical areas by the use of volatile drugs which were sealed into the canal.[6]

Alternatively, the electric current was employed in the method commonly known as ionization or electrosterilization. Here it was argued that the electric current split the electrolyte into therapeutic ions that passed through the canal into the adjacent tissues, which they were supposed to sterilize and treat.[1, 4, 13]

Only very few authors considered it important to try to influence the periapical tissues directly and to view this as a separate and distinct phase in the procedure of root canal therapy.

Thus, Walkhoff[12] advocated the filling of granulomas with his paste, which consisted of a sterilized iodoform paste as the vehicle for a carefully blended mixture of parachlorphenol-camphor-menthol.

Prader[8, 9] showed that effective sterilization and sealing of the infected root canals was not always sufficient to produce healing of the periapical tissues, especially when the granuloma had assumed a certain size or when resorptions of the apex had taken place. He ascribed this to the inflammation of the granuloma, which had a tendency to assume an independent character. Thus, certain drugs were satisfactory as sterilizing agents, yet increased the inflammatory process in the granuloma and tended to favor the central dissolution of the tissues. Furthermore, the apex which, due to the reactive procedure, was denuded because the periodontal membrane had been destroyed, acted as a foreign body irritant and delayed or prevented satisfactory restitution of anatomic conditions. Prader therefore suggested that treatment of teeth with chronic periapical involvement be divided into two distinct phases. (1) treatment of the canal and (2) periodic filling of the granuloma with a resorbable paste which combats inflammation (Apicoflux).

METHODS

This article deals with the conservative treatment of teeth with extensive periapical involvement. The cases selected were those in which root resection or even tooth extraction normally would have been considered necessary.

In general, the procedure advocated by Prader[9] was followed. This consisted of three distinct phases:

1. *Treatment of the canal.* The usual methods of thorough mechanical workup, hot syringing, and sterilization by drugs were employed until two successive negative cultures were obtained.

2. *Periodic filling of the granuloma.* At weekly intervals thereafter, an attempt was made to fill the entire granuloma through the apex as completely as possible. Apicoflux (De Trey) was used as a vehicle for a varying amount of iodoform, which was incorporated into the paste. While at the first sitting 1 part of the iodoform was used for 2 parts Apicoflux, this ratio was gradually increased to 1:1 and finally to 2:1. The paste was introduced into the canal with a rotary root canal filler (Lentullo) and worked up into the periapical area. Afterward, temporary stopping was used to seal the entrance into the canal and pressure was exerted with a plugger, which tended to transport the paste further over the apex.

Roentgenograms were taken immediately after each filling to ascertain how far the paste had been introduced, as well as immediately before the next filling to follow the speed of resorption of the paste.

As many sittings as were required to obtain a complete filling of the granuloma were held. Once the granuloma was completely filled, the third step—root canal filling—took place.

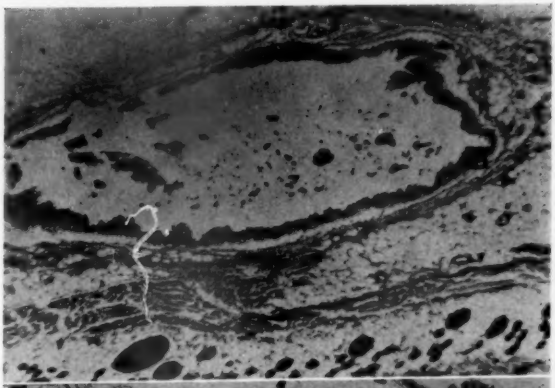
3. *Root canal filling.* The root canal was filled in the standard manner with a compact, nonresorbable, nonirritating material. Oxyphosphate cement was used, with small additions of iodoform and paraformaldehyde ("Viennese" school), and gutta-percha points were employed. Lateral condensation was used.

Period x-ray checkups were then made in order to ascertain the amount of healing and the rate at which this took place.

MATERIAL

Chemical Composition of Apicoflux (De Trey).—According to Prader,[7] Apicoflux consists of a paste which serves as a vehicle and two active substances—an antiseptic and a chemotherapeutic. The paste contains neither water nor alcohol. It melts at body temperature in the canal and moves to the apex by capillary attraction. The antiseptic belongs to the phenyl-mercury borate group; the chemotherapeutic substance is a sulfanilamide (N_1-dimethylacoyl-sulfanilamide).

Tissue Reaction to Apicoflux.—In order that the reaction of tissues to Apicoflux, or to a mixture of Apicoflux plus iodoform might be ascertained, these



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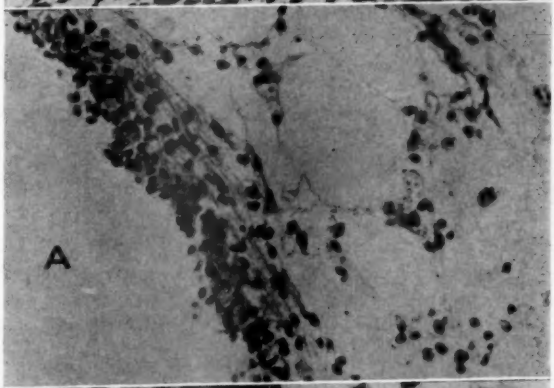


Fig. 2.

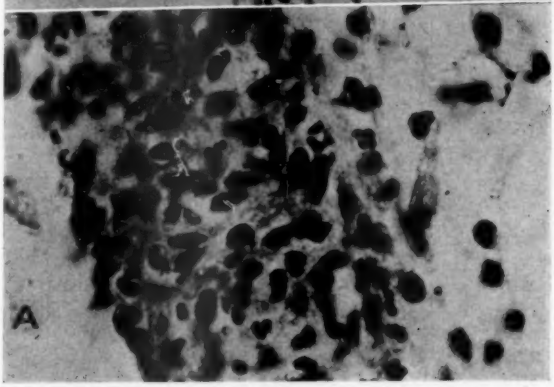


Fig. 3.

Fig. 1.—Photomicrograph of biopsy specimen of dorsal connective tissue of albino rat forty-eight hours after injection of Apicoflux. (Hematoxylin and eosin stain. Magnification, ×35; reduced ¼.)

Fig. 2.—Higher-power view of the wall surrounding the Apicoflux. (Hematoxylin and eosin stain. Magnification, ×430; reduced ¼.)

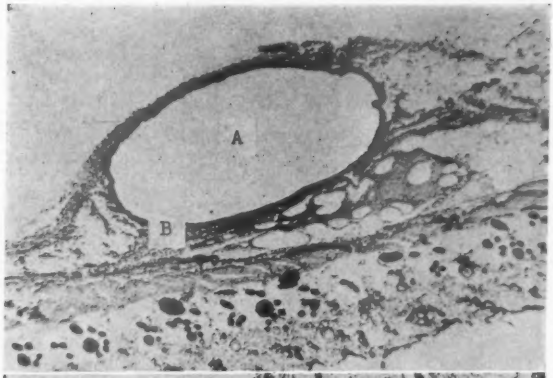
Fig. 3.—Oil-immersion photomicrograph of wall surrounding depot of Apicoflux, giving details of its cellular components. (Hematoxylin and eosin stain. Magnification, ×970; reduced ¼.)

Key to Symbols:

A, Place occupied by Apicoflux.

B, Tissue reaction around depot.

Fig. 4.



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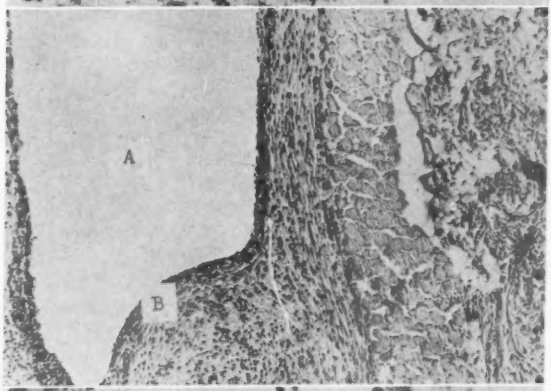

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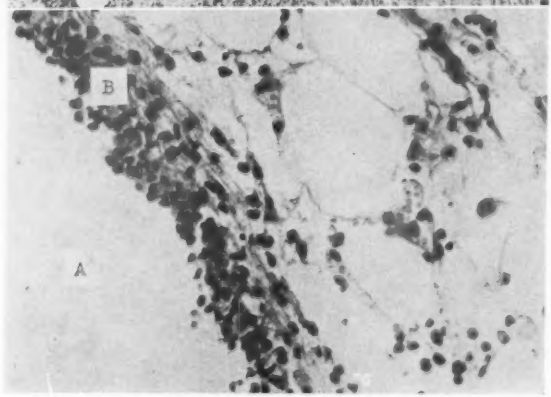

Fig. 4.—Photomicrograph of biopsy specimen of dorsal connective tissue of albino rat seven days after injection of Apicoflux. (Hematoxylin and eosin stain. Magnification, ×35; reduced ¼.)

Fig. 5.—More detailed view of tissue reaction around the depot. (Hematoxylin and eosin stain. Magnification, ×100; reduced ¼.)

Fig. 6.—Higher-power view of wall. (Hematoxylin and eosin stain. Magnification, ×430; reduced ¼.)

Key to Symbols:

A, Place occupied by Apicoflux.

B, Pyogenic membrane formed around the depot.

were injected into the dorsal subcutaneous connective tissue of albino rats. The animals were sacrificed forty-eight hours, seven days, and fourteen days after injection of the material, and the tissues were subjected to histologic studies.

After forty-eight hours, an inflammatory reaction of medium severity could be noticed. The photomicrographs show the development of a pyogenic membrane around the depot of Apicoflux. Both granulocytes and histiocytes can be noticed in it; some of the latter have a foamy appearance (Figs. 1, 2, and 3).

Fig. 7.

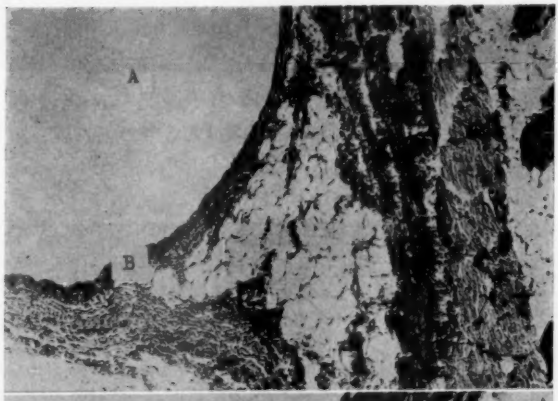

Fig. 8.

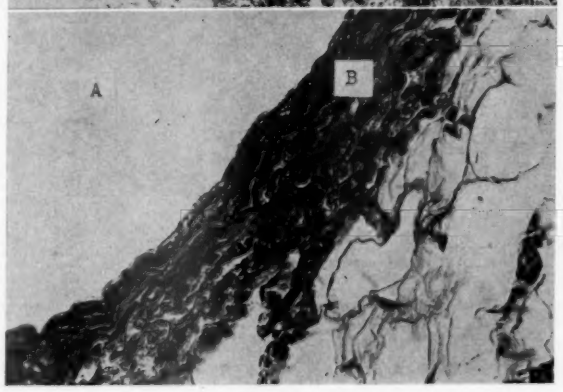

Fig. 7.—Photomicrograph of biopsy specimen of dorsal connective tissue of albino rat fourteen days after injection of Apicoflux. (Mallory's connective-tissue stain. Magnification, ×100; reduced ¼.)

Fig. 8.—High-power view of specimen shown in Fig. 7 giving details of fibrous nature of capsule. (Mallory's connective-tissue stain. Magnification, ×430; reduced ¼.)

Key to Symbols:

A, Place occupied by Apicoflux.

B, Tissue reaction, walling off the depot.

The seven-day specimen presented a similar appearance (Figs. 4, 5, and 6). However, the acute character of the reaction had decreased, and the elements of chronic inflammation were more numerous. The number of foam cells had equally increased.

After fourteen days a fibrous capsule had formed around the depot of Apicoflux (Figs. 7 and 8).

RESULTS

In no case did an unfavorable reaction take place. No pains were reported by the patients, and no sensitivity to the drugs employed was noticed.

As the roentgenograms of some of the cases treated show, healing took place rather rapidly in relation to the size of the pathologic area, and full restitution to a normal anatomic pattern was obtained (Figs. 9 to 16).

DISCUSSION

The direct treatment of periapically involved areas with a resorbable therapeutic paste seems to be helpful in bringing these areas more speedily to resolution.

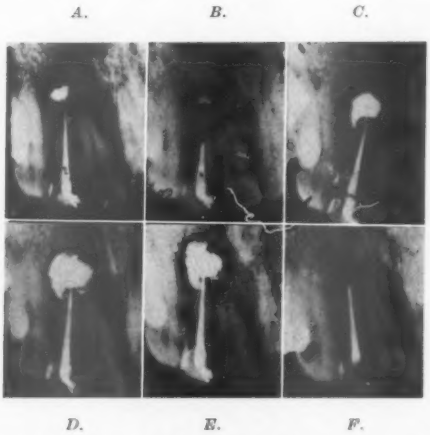

Fig. 9.—Diffuse granuloma the size of a cherry stone surrounding root of upper right lateral incisor. Unfortunately, the preoperative roentgenogram was lost, but the size of the lesion can be seen clearly in all the other views. *A*, First application of Apicoflux-Iodoform mixture. *B*, One week later. *C*, Third application. *D*, Fifth application. *E*, Filling of granuloma with Apicoflux mixture and filling of root canal with medicated oxyphosphate cement and gutta-percha points. *F*, Two years later.

The fact that treatment with Apicoflux without filling of the root canal, which is considered an essential part of other endodontic procedures, could reduce periapical pathology considerably was brought to light by several accidental findings.

In one case, a patient who had received the first application of Apicoflux interrupted treatment for several months. When he finally returned, the roentgenograms showed marked improvement (Fig. 17).

These findings seem to confirm Prader's theory that the denuded apex acts as a foreign body; surrounding and covering it with a beneficial "wound salve" is sufficient to initiate the process of healing, even without filling the root canal itself.

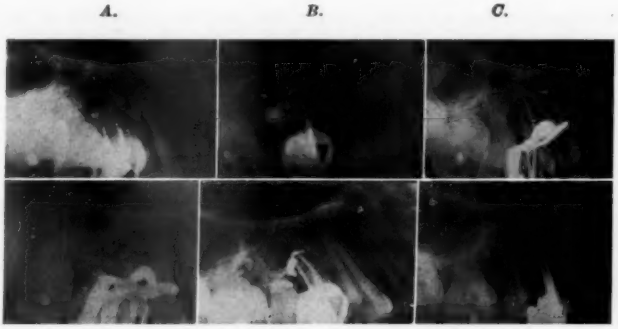

Fig. 10.—Granuloma and considerable resorption of apex of upper right first premolar. *A*, Preoperative view. *B*, Second application of Apicoflux mixture. A copper band has been cemented around the tooth for better isolation. *C*, Trial of gutta-percha points. *D*, Gutta-percha points adjusted to proper length. *E*, Filling of granuloma and canals. *F*, Two years later.

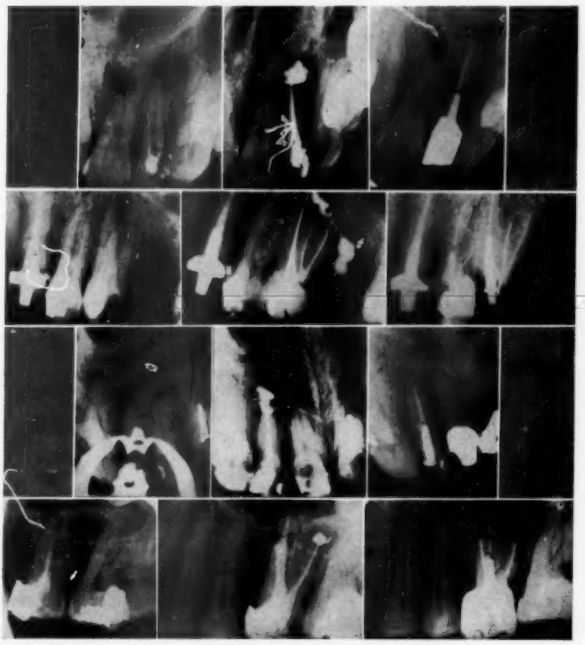

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 14.

Fig. 11.—Extensive granuloma surrounding root of upper left lateral incisor. *A*, Preoperative roentgenogram. *B*, Root canal filling. *C*, Five years later.

Fig. 12.—Upper left second premolar. Note three roots with pathologic changes and fistulous opening. *A*, Preoperative view. *B*, Root canal filling; the Apicoflux mixture traversed the fistula and exuded from the gingiva. *C*, Two years later.

Fig. 13.—Upper right lateral incisor with circumscribed granuloma. *A*, Preoperative roentgenogram. *B*, Root canal filling. *C*, Four years later.

Fig. 14.—Upper left first molar with granulomas on all three roots. *A*, Preoperative roentgenogram. *B*, Root canal filling. *C*, Two years later; the areas on the mesial and buccal roots have already healed completely; the granuloma on the distal root has decreased considerably.

In our experimental animals, tissue reaction to Apicofluv or to a mixture of Apicoflux and iodoform was stronger than those found by Prader[10] in rabbits. It is possible that the difference in the laboratory animals could account for this discrepancy.

Fig. 15.

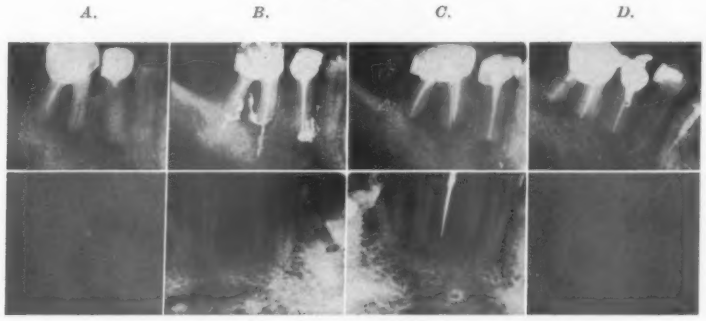

Fig. 16.

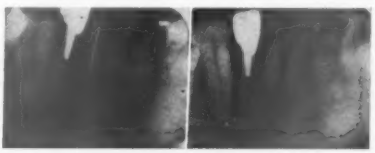

Fig. 15.—Lower right second premolar and first molar. *A*, Preoperative view. *B*, Application of Apicoflux; note penetration into bifurcation area. *C*, Filling of root canals. *D*, Two years later.

Fig. 16.—Lower right central incisor. *A*, Preoperative roentgenogram. *B*, Eleven months after filling of root canal. (Case courtesy of Dr. A. Sarnat.)

Fig. 17.—Severe periapical involvement of lower right central incisor. *A*, Root canal was measured during treatment. After application of Apicoflux, treatment was interrupted for about five months. *B*, Control roentgenogram taken five months later when treatment was resumed. Considerable improvement can be seen, and regeneration of bone has taken place in spite of the fact that the root canal was not filled. (Case courtesy of Dr. A. Sarnat.)

CONCLUSION

By adding another phase—direct treatment of the areas of periapical involvement—to endodontic treatment, it is possible to treat conservatively cases in which it previously was thought that only surgery could produce satisfactory results. This method is especially valuable in cases in which anatomic conditions make surgery impractical or in which surgery is contraindicated for psychological or medical reasons.

The author wishes to express his thanks to Mrs. Ch. Salomon who made all the photographs used in this article.

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HISTOCHEMICAL STUDY OF PULP HEALING

R. L. Cabrini, M.D., O. A. Maisto, D.D.S., and E. E. Manfredi, D.D.S.,
Buenos Aires, Argentina

THE action of alkaline phosphatase, mucopolysaccharides, and glycogen in the process of pulp healing has been studied. For this purpose, healthy or normal pulp of fifteen human teeth has been used. The pulp chambers of five teeth were perforated and capped with calcium hydroxide; five other teeth were also perforated and capped with zinc oxide-eugenol; and the last five normal teeth were kept as untreated controls.

The teeth were extracted after fifteen and thirty days. During this period the new dentine starts to form in the teeth treated with calcium hydroxide.[1, 2] After the tooth was fractured, the pulp was extracted and fixed in 80 per cent alcohol at 4° C. It was embedded in paraffin, and alkaline phosphatase was demonstrated by Gomori's method; mucopolysaccharides were demonstrated by the PAS method of McManus. Controls were treated with ptyalin.

The alkaline phosphatase reaction of pulp wounds increases slightly. No differences were detected between teeth treated with calcium hydroxide and those treated with zinc oxide-eugenol.[3, 4] On the other hand, all teeth treated with calcium hydroxide showed large amounts of PAS-positive granules in newly formed odontoblasts, preodontoblasts, and pulp cells of the healing and adjacent areas. No changes were seen in control teeth or in teeth treated with zinc oxide-eugenol. These PAS-positive granules were removed by ptyalin, which showed them to be glycogen.

SUMMARY

The results of this study indicate that the histochemical demonstration of glycogen gives useful evidence of pulp healing if we admit that most pulps treated with calcium hydroxide heal with new formation of dentine, whereas those treated with zinc oxide-eugenol do not.[1, 2, 5] On the other hand, these results confirm the importance that glycogen seems to have in the formation of tissues with a calcified matrix.[6]

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RESEARCH

RESPONSE OF THE PERIODONTIUM, PULP, AND SALIVARY GLANDS TO GINGIVAL AND TOOTH INJURY IN YOUNG ADULT MALE RATS

III. Submaxillary Glands

S. S. Stahl, D.D.S., M.S., New York, N. Y.*

RAT salivary glands have been shown to respond to the stimulation of various hormones as well as to stress. Hypophysectomy,[1] propylthiouracil administration,[2] and the introduction of stressors,[3, 4] such as formaldehyde injection and colchicine, have resulted in a reduction in size and granular contents of the intralobular ducts and a reduction in secretory granules of the acini. These changes were seen primarily in the submaxillary glands. Degenerative changes in the intralobular ducts of the submaxillary glands have also been noted in rats bearing malignant abdominal tumors.[5] Sreebny[1] has shown a proteolytic enzyme to be contained in the granules of the intralobular ducts.

The present investigation attempted to study changes in rat submaxillary glands associated with an experimentally induced gingival and pulpal injury.

METHODS AND MATERIALS

Experimental animals and experimental procedures have been described previously.[6] Whenever possible, animals were sacrificed in the early forenoon in order that salivary glands might be obtained at comparable rates of secretory activity.

OBSERVATIONS

The most pronounced changes observed in the salivary glands were those seen in the intralobular ducts of the submaxillary glands. The intralobular

From the Murry and Leonie Guggenheim Foundation, Institute for Dental Research, and the Department of Periodontia and Oral Medicine, New York University College of Dentistry.

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*Assistant Professor, Department of Periodontia and Oral Medicine, New York University.

Fig. 1.

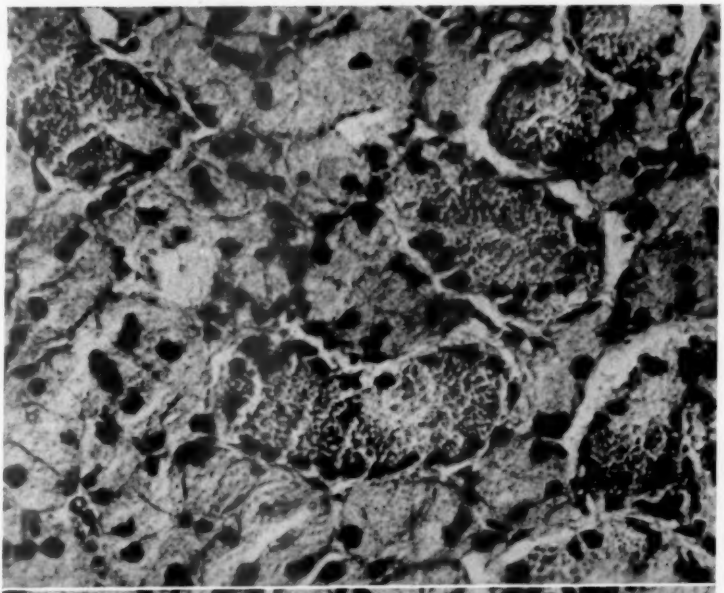

Fig. 2.

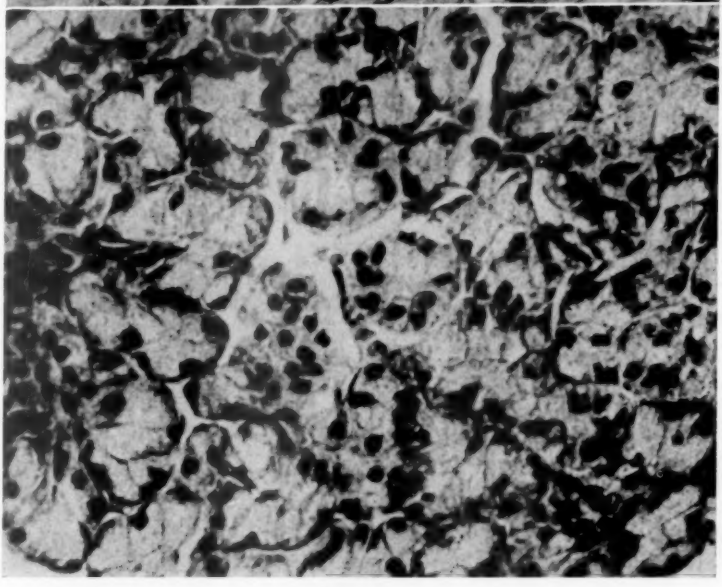

Fig. 1.—Photomicrograph of a section of the submaxillary gland of a noninjured rat. (Hematoxylin and eosin stain. Magnification, ×550.)

Fig. 2.—Photomicrograph of a section of the submaxillary gland of a rat sacrificed six hours after dental injury. (Hematoxylin and eosin stain. Magnification, ×550.)

Fig. 3.

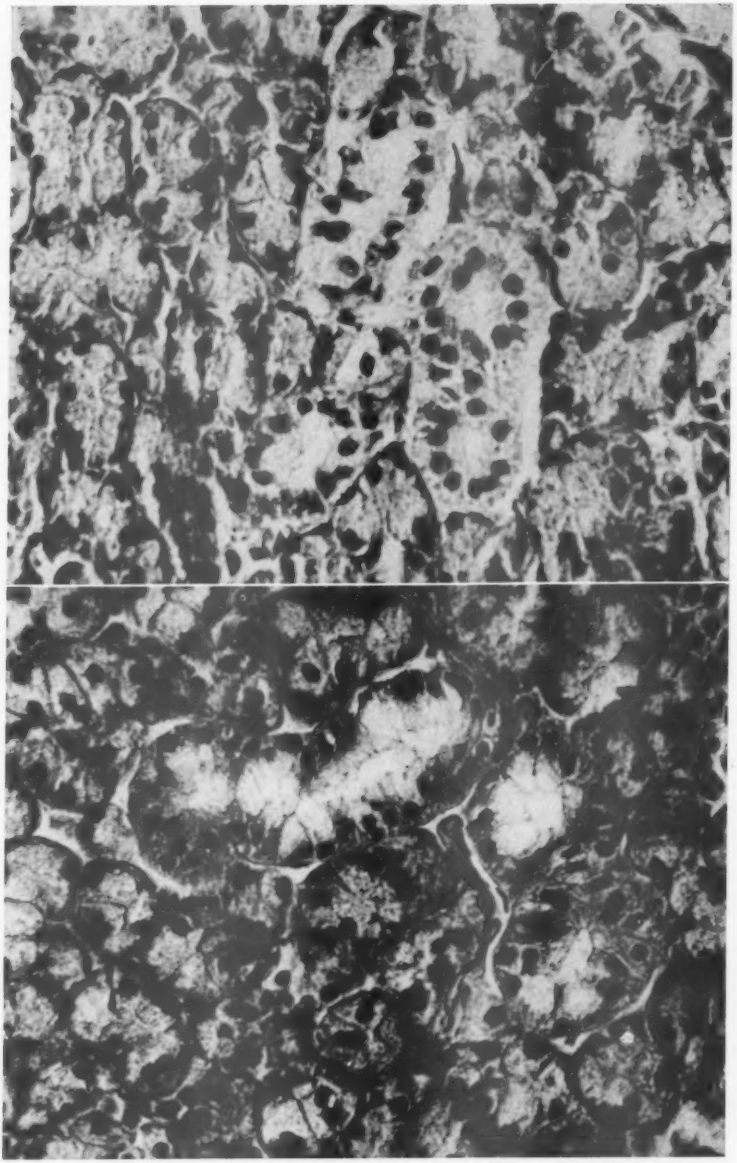

Fig. 4.

Fig. 3.—Photomicrograph of a section of the submaxillary gland of a rat sacrificed forty-eight hours after dental injury. (Hematoxylin and eosin stain. Magnification, ×550.)

Fig. 4.—Photomicrograph of a section of the submaxillary gland of a rat sacrificed ten days after dental injury. (Hematoxylin and eosin stain. Magnification, ×550.)

Fig. 5.

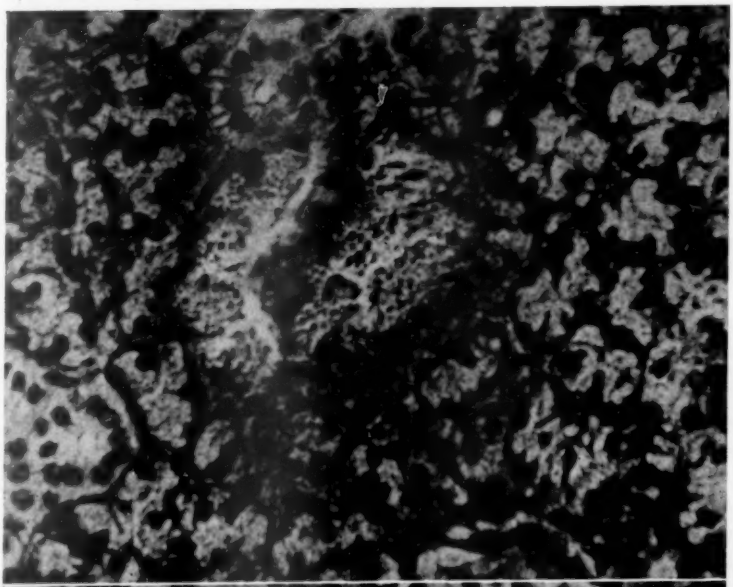

Fig. 6.

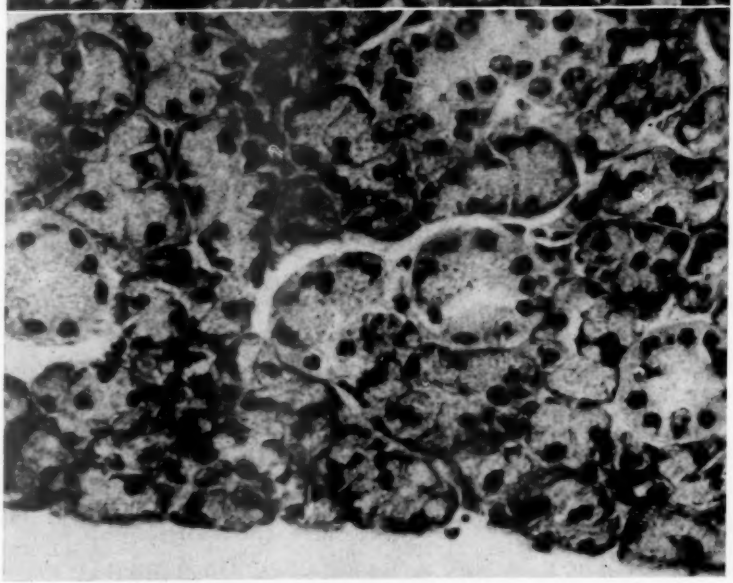

Fig. 5.—Photomicrograph of a section of the submaxillary gland of a rat sacrificed twenty-two days after dental injury. (Hematoxylin and eosin stain. Magnification, ×550.)

Fig. 6.—Photomicrograph of a section of the submaxillary gland of a rat sacrificed thirty-three days after dental injury. (Hematoxylin and eosin stain. Magnification, ×550.)

ducts of noninjured animals appeared crowded with granules (Fig. 1). Between three and six hours after the gingival injury, a slight reduction in granules was noted (Fig. 2). This decrease in granules became more evident after forty-eight hours following injury (Fig. 3) and continued to be seen in specimens two to fourteen days after injury (Fig. 4). The ducts of these specimens also seemed to be decreased in number, and their cytoplasm appeared vacuolated. The acini stained less deeply, but acinar changes were less striking than those seen in the intralobular ducts.

An increase in eosinophilic granules in the intralobular ducts was noted in specimens obtained twenty-one days after injury (Fig. 5) and continued to be present in most of the older specimens (Fig. 6).

COMMENT

The decrease in eosinophilic granules of the intralobular ducts followed gingival injury and became marked as the inflammatory changes increased at the wound site. As the dental injury healed, the granular content of the ducts increased and continued to be quite evident in most of the specimens studied. Thus, the changes in duct granularity may reflect a general stress response following local injury or the specific response to a dental injury, or they may represent a combination of both factors. Further studies are necessary to clarify the role of salivary gland activity in oral injury.

SUMMARY AND CONCLUSIONS

Following dental injury, a decrease in the granular content of the intralobular ducts of the submaxillary glands was observed. The decrease was first noted three hours after injury and became more marked in the specimens obtained forty-eight hours after injury. The decrease in granules continued to be evident in specimens taken up to fourteen days after injury, after which time the granular content gradually increased.

The author wishes to thank O. Joly, D.D.S., and Helen Rosenman, B.A., for their cooperation in the preparation of these studies.

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THE EFFECT OF PAROTID GLAND EXTRACT ON THE HARD AND SOFT TISSUES OF GROWING MICE

Giuliano Quintarelli, M.D., D.M.D., Robert B. Gordon, M.D.,** and Howard H. Chauncey, Ph.D.,* Boston, Mass., and New York, N. Y.*

IT HAS been postulated that the salivary glands produce an internal secretion.[1, 5, 7, 11, 12] This endocrine-like function has been partially substantiated by clinical and experimental findings.[8] Certain investigators have stated that a deficiency in salivary gland activity is capable of inducing changes in the structure of tissues of mesenchymal origin.[7] This belief is based on the observation that experimental asialadenism results in degeneration of epiphyseal cartilaginous cells and retarded calcification in the long bones. The teeth of asialadenic animals exhibited a widening of the predentine layer, degeneration of enamel cells, and an abnormal degree of cementum resorption, while in hypersialadenism supplemental parotid gland extract administered parenterally resulted in hypertrophic dentine and increased cementum deposition.[10] On the other hand, many competent workers[2, 3, 6, 9, 13, 14] have expressed the opinion, based on experimental observations, that these glands do not have an endocrine function. This dichotomy of opinion prompted the following investigation, which was undertaken to determine whether or not excessive doses of the aforementioned extract could induce changes in the normal growth pattern of the hard and soft tissues of young mice. It was felt that an investigation of this nature would at least provide a toxicologic basis for further inquiries into the physiologic action of parotid gland extracts.

METHODS AND MATERIALS

Thirty mice, from 4 to 6 weeks of age and weighing approximately 25 grams each, were divided into three groups: experimental (I), sham (II), and control (III). Group I, composed of fourteen animals (seven males and seven females), received salivary gland extract (Parotin†). The test material, a water-soluble protein obtained from bovine parotid glands, was prepared as

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*Department of Dental Research, Tufts University School of Dental Medicine, Boston, Massachusetts. (Dr. Quintarelli is now at the University of Alabama School of Dentistry, Birmingham, Alabama.)

**Department of Orthopedic Surgery, New York University, Bellevue Medical Center, New York, New York.

†Supplied through the courtesy of the Teikoku Hormone Mfg. Co., Ltd., Tokyo, Japan.

a 1 mg./ml. solution in physiologic saline. The dosage used was 0.5 mg. twice weekly for four weeks, followed by 1.0 mg. twice a week for the next five weeks. The experimental animals (Group I) thus received a total dose of 14 mg. per animal over the nine-week period. The extract was administered by intraperitoneal injection. The animals in Group II (four males and four females) received an equivalent volume of saline, while those making up Group III (also four males and four females) were untreated. The weight of each animal was recorded twice a week immediately prior to injection of the extract. After nine weeks all animals were sacrificed by light anesthesia (ether) and decapitation. The rear joints, adrenal glands, salivary glands, gonads, mandibles and representative sections of skin and aorta were removed and placed in Bouin's fixative. A histologic examination was made, using hematoxylin and eosin, Masson's trichrome, and Weigert's elastin stains.

RESULTS AND DISCUSSION

The animals behaved normally throughout the test period, and no substantial difference in weight gain was noted among the three groups. All animals appeared healthy, and there were no premature deaths in any of the groups. The hard tissues (bone and teeth) and periodontal membranes of the experimental group did not differ from similar tissues obtained from the animals of the sham and control groups. There was no apparent difference in cementum apposition or noticeable increase in the calcification of epiphyseal cartilage. Similarly, testes, ovaries, adrenals, salivary glands, skin, and aorta all appeared normal. Thus, the hard and soft tissues of the experimental group did not differ from identical tissues examined from animals in the sham and control groups.

No definite conclusions concerning the possible endocrine action of salivary gland extract (Parotin) can be drawn from the results herein presented. The hypertrophic changes in cartilaginous and hard tissues observed by previous investigators[10] did not occur after daily injection of 0.3 mg. of Parotin per 100 grams of body weight for two months (equivalent to 21 mg. per kilogram per week). The dosage employed in the present study was 30 mg. per kilogram per week for four weeks, followed by 60 mg. per kilogram per week for five weeks. Not only is this in excess of the recommended therapeutic dose of 3.0 mg. per kilogram of body weight per week,[8] but it also exceeds the amount that other investigators[10] have deemed sufficient to produce hypertrophic changes. If this material does have a hormonelike action which influences growth, this action is not evidenced when the material is administered in the above-stated doses to normal-growing mice. As for the toxicity, the material appeared innocuous even though the amount administered was ten to twenty times greater than the recommended therapeutic dose.

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PAROTID FLUID AS A MEDIUM FOR THE DETERMINATION OF HUMAN ADRENOCORTICAL STATUS

Ira L. Shannon, Major, USAF (DC), and
John R. Prigmore, Captain, USAF (MSC)

MEASUREMENT of the concentration of adrenocortical steroids, or their degradation products, in body fluids provides a sensitive approach to the study of adrenal cortical function. Thus, reliance is placed upon such findings in hypo- and hyper- diseases of the cortex as well as in endogenous hyperactivity states resulting from stress.

Studies of adrenocortical steroid concentration have been almost completely confined to blood and urine. In this article we shall describe results obtained from the analysis of human parotid fluid and serum for free (nonconjugated) 17-hydroxycorticosteroids (17-OHCS) and of urine for total 17-OHCS, before and after the oral administration of synthetic adrenocortical analogues. We used the drugs to alter serum and urine corticoid levels in order that we might ascertain whether the concentration of parotid fluid 17-OHCS would undergo concomitant changes.

PROCEDURE

The subjects were healthy young men between 17 and 22 years of age who recently had been found physically qualified for military service. Environmental exposure was virtually identical for all subjects, as were mealtimes, types of food ingested, and times of arising and retiring. Blood was collected by venipuncture, and the serum was retained. Parotid fluid was collected by dual-chambered vacuum cap under the stimulation of 3.0 grams of sugared gum*; a clearance (acquaintance) sample was collected prior to each test collection. Parotid fluid and blood samples were collected immediately prior to the

From the Dental Sciences Group (I. L. S.) and the Medical Sciences Division (J. R. P.), School of Aviation Medicine, United States Air Force, Brooks Air Force Base, Texas.

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*Furnished by Dr. Robert Heggie, American Chicle Company.

oral administration of 50 mg. of the drug under study, and subsequent collections of both fluids were made two, four, and six hours after the drug was administered. Subjects force-voided at time 0, and urine was collected as a single sample covering the entire six-hour experimental period. No food was allowed from three hours prior to drug administration until completion of the experiment.

The concentration of free 17-OHCS in parotid fluid and in serum was determined by the method of Peterson and associates,[1] which involves a methylene chloride extraction procedure. Total 17-OHCS levels in urine were analyzed by the butanol extraction method of Reddy.[2] Both techniques employ the Porter-Silber[3] color reaction between phenylhydrazine and 17,21-dihydroxy-20-ketosteroids.

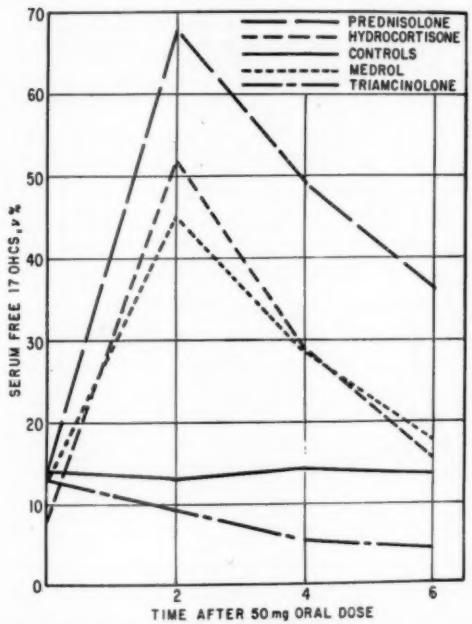

Fig. 1.—Free 17-hydroxycorticosteroid levels in serum following the oral administration of synthetic analogues of hydrocortisone.

Four experimental groups were studied. Each group included eight subjects given a 50 mg. drug dose orally and four participants who served as untreated controls. A total of sixteen control subjects were studied, and the results were grouped for the final control base lines. The drugs* employed were hydrocortisone, prednisolone (delta-1 hydrocortisone), Medrol (delta-1, 6-methyl hydrocortisone), and triamcinolone (delta-1, 9-alpha-fluoro, 16-hydroxy hydrocortisone).

*Drugs employed in this study were furnished by the Upjohn Company, Lederle Laboratories, and Merck, Sharp & Dohme.

RESULTS AND DISCUSSION

Prednisolone, hydrocortisone, and Medrol produced marked increases in free 17-OHCS in serum (Fig. 1). Prednisolone prompted the greatest rise, with a peak level some 4.5 times that of predrug levels. All three drug groups peaked at the two-hour sampling time. Control subjects demonstrated no change in levels with the passage of time, while triamcinolone produced a decrease in serum 17-OHCS levels. As shown in Fig. 2, free 17-OHCS levels in parotid fluid very closely paralleled the levels in serum. Prednisolone, hydrocortisone, and Medrol caused marked increases in levels, the rise following prednisolone being approximately fivefold. Again, triamcinolone led to a depression of free steroid levels.

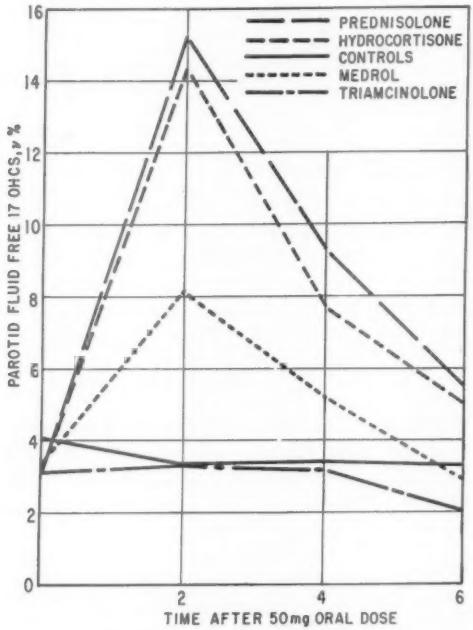

Fig. 2.—Free 17-hydroxycorticosteroid levels in parotid fluid following the oral administration of synthetic analogues of hydrocortisone.

The decreased concentration associated with triamcinolone dosage was due to the fact that this preparation, unlike the other drugs under study, does not give a Porter-Silber color reaction. Although it has the basic structure said to be necessary for the reaction (17,21-dihydroxy-20-ketosteroid), this drug, when dissolved in slightly acid water, gives a negative Porter-Silber response. That triamcinolone does not give a Porter-Silber reaction with phenylhydrazine in sulfuric acid has been reported by Walser and Schlunke[4] and by Hatfield and

Shuster.[5] The OH group at C-16 is definitely implicated, since the methyl group at C-16 in Decadron (delta-1, 9-alpha-fluoro, 16-methyl hydrocortisone) does not interfere with the color reaction. This Decadron conformation to the Porter-Silber reaction, confirmed in our laboratories, has been previously reported.[4] Thus, it becomes apparent that triamcinolone, since not determinable by the phenylhydrazine reaction, produces a drop in measurable 17-OHCS by suppression of endogenous adrenocortical secretion.

Prednisolone administration prompted a urine total (free plus conjugated) 17-OHCS excretion averaging 1.85 mg. per hour over the six-hour sampling period, compared to an average excretion of 0.40 mg. per hour in untreated controls. As with serum and parotid fluid, marked increases also followed administration of Medrol and hydrocortisone, the 17-OHCS excretion values averaging 1.47 mg. per hour and 1.27 mg. per hour, respectively. The urine 17-OHCS concentration following triamcinolone was less than in the control subjects (0.38 mg. per hour as compared to the control excretion of 0.40 mg. per hour), but it was not depressed as much as the equivalent level in serum and in parotid fluid. This would suggest an effect on conjugation rate, since the urine method measures both free and conjugated forms while free 17-OHCS alone is measured in serum and parotid fluid.

The findings of the present study, coupled with previous results following intramuscular injection[6, 7] and intravenous infusion[8] of adrenocorticotropin, substantiate our basic premise that the steroid concentration in parotid fluid may well be used as an indicator of adrenocortical status. In contrast to the problems inherent in multiple blood sampling, continuous parotid sampling is possible, since the parotid cap may be left in place for an extended period of time. Sampling periods of up to three hours of continuous stimulation showed no diminution in parotid fluid 17-OHCS concentration. Further, the steroid concentration appears independent of parotid flow rates. Comparable steroid levels were found in whole saliva, but parotid sampling is much more desirable from the point of view of pipetting preciseness, bacterial contamination, content of sloughing tissue, and response to storage methods.

Studies utilizing parotid fluid 17-OHCS levels are also of particular value to those investigators who require a sampling method that is adaptable to very restricted operating quarters, such as hypersonic fighter aircraft and space-flight simulators, and is completely devoid of stressful influences.

SUMMARY

Oral administration of synthetic analogues of hydrocortisone and subsequent comparison of parotid fluid, serum, and urine 17-OHCS levels indicated that free 17-OHCS levels in parotid fluid would serve well as indicators of human adrenocortical status.

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STUDIES ON THE SURVIVAL OF PARENTERALLY INOCULATED ORAL TREPONEMES IN THE GUINEA PIG

R. J. Fitzgerald, Ph.D., E. G. Hampp, D.D.S., M.S., and H. R. Stanley, D.D.S., M.S., Bethesda, Md.*

THE role of the spirochetes in the fusospirochetal diseases still remains undetermined. Although these organisms are characteristically present in the lesions of ulcerative gingivostomatitis, many other types of microorganisms are also present to complicate the picture. Furthermore, the same types of spirochetes may be found on the gingivae of some persons in whom no pathologic condition is evident. Early attempts to discover the etiology of this condition through studies in experimental animals led to the generally accepted conclusion that it was a mixed infection. However, there was considerable disagreement over the number and types of microorganisms which were essential for the establishment of the infection. Rosebury and associates[1-3] have reviewed and extended the early studies in experimental animals. In a carefully controlled series of experiments involving the recombination of twenty-nine bacterial cultures and five spirochetal cultures these workers were unable to elicit in guinea pigs responses that could be considered comparable to the infection obtained with fusospirochetal exudate.[3] Macdonald and colleagues[4] later were able to obtain typical "fusospirochetal" abscesses in guinea pigs by using the "wheel plate" technique to recombine sixteen bacterial strains and a spirochete culture in which *Treponema microdentium* predominated. Some of Macdonald's bacterial strains differed from those used by Rosebury, notably two Bacteroides strains and a gram-negative motile rod. Recently Macdonald and associates[5] have reported the production of typical "fusospirochetal" abscesses in guinea pigs inoculated subcutaneously in the groin with a mixture of only four pure strains of bacteria: two strains of Bacteroides, a motile gram-negative anaerobic rod, and a diphtheroid. Their criteria for "fusospirochetal" infection included abscess formation, the color and odor of the exudate, and the histologic appearance of the walls of the abscess. Neither spirochetes nor fusiform bacteria were essential in this test system, although, when added, they apparently survived and multiplied.

From the National Institute of Dental Research, National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare.

*Senior Research Associate, American Dental Association, at the National Institute of Dental Research, National Institutes of Health.

Attempts to infect germ-free or cortisone-treated guinea pigs by subcutaneous or intraperitoneal inoculation with single or combined strains of a small oral treponeme, *Borrelia vincentii* or *Borrelia buccale*, were not successful[6] in spite of the fact that the cortisone-treated animal and the germ-free animal are known to exhibit reduced host defense mechanisms.[7-12]

Indications that the spirochetes may have some pathologic potential, however, may be found in the recent report of Hampp and Mergenhagen,[13] who produced localized abscesses in rabbits by the intracutaneous injection of pure cultures of *Borrelia vincentii, Borrelia buccale,* and small oral treponemes. Histologic studies of Vincent's infection in human patients have also revealed spirochetes penetrating well in advance of the lesion,[14-16] and spirochetes have been isolated from unexposed nonvital pulps of human teeth.[17]

In the present study a new attempt was made to infect germ-free guinea pigs with either of two additional strains of small oral treponemes. In addition, a time study was performed to investigate the survival of small oral treponemes injected intramuscularly in the conventional (not germ-free) guinea pig.

EXPERIMENTAL

For the experiments involving germ-free guinea pigs, small oral treponeme strains, EH and E45, were employed. Strain EH was freshly isolated from a clinically normal mouth, and strain E45 was a gas-producing spirochete isolated from an unexposed nonvital pulp canal.[17] For inoculation, the organisms were grown for three days in a modified Huntoon's medium[18-19] containing 10 per cent canine ascitic fluid and 0.1 per cent reduced glutathione. The medium also contained 1 mg. of finely ground charcoal (Darco G-60) per milliliter for marking the inoculation site in the animals.

Nine germ-free guinea pigs representing three litters obtained by cesarean section were housed in a Reyniers germ-free isolator[20] and maintained on the steam-sterilized L445 diet of Phillips and colleagues.[21] At the age of 3 weeks, three of the animals were injected intraperitoneally with 9×10^7 cells of strain EH in 1.0 ml. of the charcoal-containing growth medium. Two animals received 0.5 ml. of the same culture intramuscularly in the groin. Two animals received 14×10^7 cells of strain E45 intraperitoneally, and the last two animals received half that inoculum intramuscularly. At the same time ten normally delivered conventional guinea pigs of the same age were similarly inoculated, three intraperitoneally and two intramuscularly, with the same spirochete strains.

At the end of one week, one of the germ-free animals inoculated intramuscularly with strain EH died as a result of intestinal volvulus. There was no gross evidence at the inoculation site of an infectious process, nor could spirochetes be recovered in cultures of the charcoal-containing tissues.

Two weeks after inoculation, during which time there was no gross evidence of abscess formation, all the surviving animals were sacrificed. Samples of blood and various tissues, including the plainly visible injection site, were

cultured in the spirochete growth medium. In addition, tissues were sectioned and stained with hematoxylin and eosin and Steiner's silver stain for spirochetes. With the techniques employed, there was no evidence of an infectious process or even of survival of the spirochetes. This was true for the germ-free animals as well as the conventional control group.

The evidence from these experiments indicated that the spirochetes failed to survive and multiply in the muscle or in the peritoneal cavity of the guinea pig. Consequently, a further experiment was designed to study the viability of spirochetes and their demonstrability by dark-field examination, by culture, and in stained sections when injected intramuscularly in the conventional guinea pig.

TABLE I. SURVIVAL OF SMALL ORAL TREPONEMES IN GUINEA PIG MUSCLE DETERMINED BY VARIOUS METHODS

ANIMAL NO.	SACRIFICED (HOURS)	DARK-FIELD	CULTURE	SILVER STAIN
1	0	+	–	+
2	1	–	+	–
3	2	+	+	+
4	4	–	+	+
5	7	?*	+	–
6	24	–	–	–
7	29	–	–	–
8	48	–	–	–

*Only an occasional nonmotile spirochete present.

For this experiment, eight female guinea pigs, weighing approximately 200 grams each, were employed. Each animal was injected intramuscularly in the left thigh with 0.5 ml. of a three-day culture of the small oral treponeme strain FM grown in modified Huntoon's medium containing charcoal as previously described. The culture was estimated to contain 2.8×10^8 spirochetes per milliliter. Each animal also received in the right thigh a control injection of 0.5 ml. of uninoculated medium which also contained charcoal. Animals were sacrificed at varying times following inoculation, and portions of the tissue marked by the charcoal were removed for dark-field examination, culturing for spirochetes, and preparation of sections. The presence of the spirochetes as determined by the various methods is shown in Table I. For the dark-field examination, a plus sign (+) indicates observation of actively motile spirochetes. In the tissue of the animal sacrificed at the seventh hour, a few nonmotile spirochetes were seen. The organism was recovered in cultures up to and including the seventh hour but not later. In tissue sections stained by Steiner's method, the spirochetes were demonstrable only up to the fourth hour.

Histopathologic Findings.—Injection of the control medium containing charcoal provoked an acute inflammatory response. It was possible, however, to observe both quantitative and qualitative differences between this response and that which followed injection of the growth medium containing both spirochetes and charcoal. The findings may be summarized as follows: At two hours following the inoculations the area of inflammation had extended beyond the immediate vicinity of the charcoal particles, but the concentration

Fig. 1.

Fig. 2.

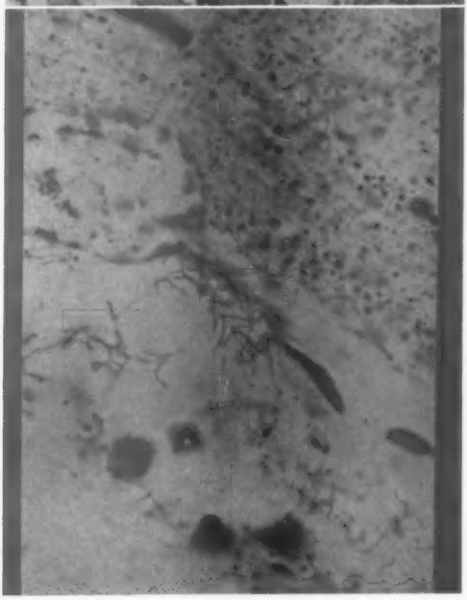

Fig. 1.—Injected muscle after two hours, showing granulocyte infiltration at inoculation site. The black particles are due to the charcoal used as a marker. (Hematoxylin and eosin stain. Magnification, ×270; reduced ⅙.)

Fig. 2.—Section from area shown in Fig. 1. Note spirochetes in a muscle bundle. (Steiner's stain. Magnification, ×1600; reduced ⅙.)

of neutrophilic granulocytes was markedly greater in the spirochete-containing tissues (Figs. 1 and 2). By the fourth hour the acute inflammatory infiltrate in the latter tissues extended into the muscle bundles (Fig. 3), whereas the granulocyte response in the controls resembled that seen at two hours in the spirochete-injected tissues and remained confined to the interstitial tissue spaces between the muscle bundles. After seven hours numerous monocytes were evident in the control sections, but only an occasional monocyte had appeared in the tissues inoculated with spirochetes. By the twenty-fourth hour, monocytes predominated in the controls and there were numerous degenerating granulocytes to be seen. In contrast, intact granulocytes predominated in the

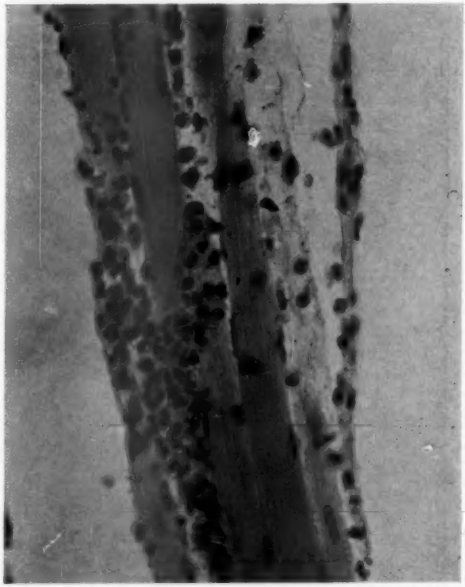

Fig. 3.—Injected muscle after four hours, showing extension of inflammatory infiltrate into the muscle bundles. (Hematoxylin and eosin stain. Magnification, ×570; reduced ⅓.)

spirochete-injected tissues, although moderate numbers of monocytes were evident. After twenty-nine hours the granulocyte still remained the predominant cell type in the spirochete-injected tissues, with an increasing number of monocytes and a few degenerating granulocytes observable. At this point, the infiltrate in the control sections consisted almost entirely of monocytes, with some macrophages and an occasional giant cell. The final control sections forty-eight hours after inoculation showed a typical foreign-body response with numerous multinucleated giant cells and only a rare neutrophilic granulocyte (Fig. 4). At this time the spirochete-inoculated tissues exhibited characteristics of early resolution, with monocytes outnumbering cells of the acute type (Fig. 5).

Fig. 4.

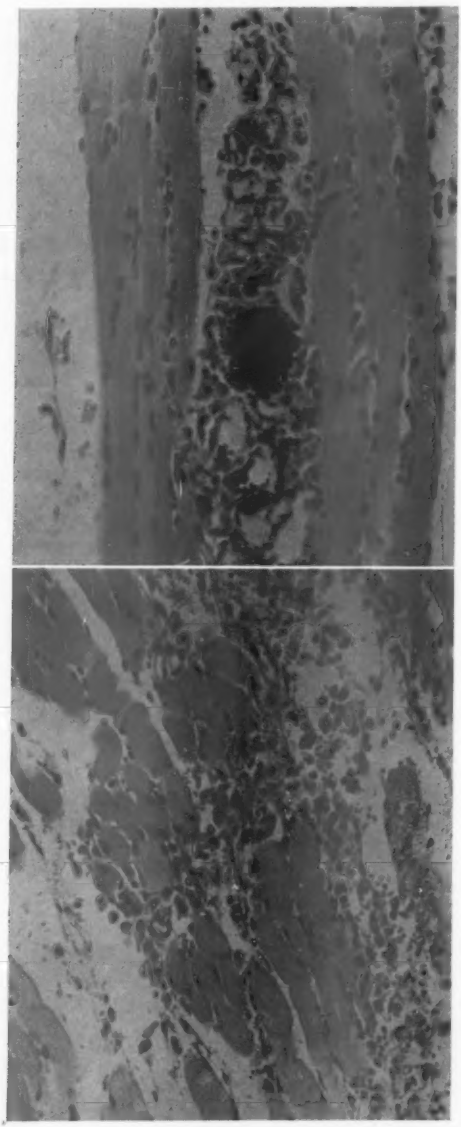

Fig. 5.

Fig. 4.—Control muscle after forty-eight hours, showing typical foreign-body response to charcoal-containing medium with numerous multinucleated giant cells evident. (Hematoxylin and eosin stain. Magnification, ×260; reduced ⅙.)

Fig. 5.—Injected muscle after forty-eight hours, showing predominance of monocytes.

DISCUSSION

The present findings confirm earlier observations[6] that pure cultures of the oral spirochetes did not survive or give rise to an infection when injected intraperitoneally or intramuscularly in the germ-free or the conventional guinea pig. Apparently, as in the case of the cortisone-treated guinea pig also,[6] the host defense mechanisms are fully adequate to cope with inoculations of between 10^7 and 10^8 spirochetes in these sites.

The presence of charcoal alone in the intramuscular inoculation menstruum provoked an acute inflammatory response which, in the conventional guinea pig, was well advanced toward resolution in twenty-four hours. In the presence of both spirochetes and charcoal, an additional twenty-four hours was required before the same degree of resolution was attained. While this would indicate that under these experimental conditions the spirochetes can induce some early signs of an infectious process, it is apparent that they were unable to persist and establish a true infection. It was well in advance of this point, namely, between the seventh and twenty-fourth hours, that spirochetes were no longer detectable in the tissues; this indicates that they die out or are killed rapidly under these conditions.

SUMMARY

Germ-free and conventional guinea pigs were inoculated intraperitoneally and intramuscularly with between 10^7 and 10^8 cells of either of two pure strains of small oral treponemes isolated from human beings. The organisms were inoculated in their growth medium, which contained a small amount of charcoal as a marker for the inoculation site. After two weeks there was no evidence of infection, and spirochetes could not be recovered in cultures or observed in sections of the inoculation sites. A time study of intramuscular inoculation in conventional guinea pigs of 10^8 cells of a third small oral treponeme in charcoal-containing medium revealed that under these conditions the spirochetes provoked the early histologic response of a typical acute and diffuse inflammatory lesion which, however, was well on the way to resolution within forty-eight hours. Twenty-four hours after inoculation viable spirochetes no longer could be demonstrated in the tissues by microscopic examination or recovered in cultures of the inoculation site.

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ANNOUNCEMENTS

American Association of Endodontists

The American Association of Endodontists will sponsor a symposium entitled "Biology of Dental Pulp" on Thursday, Feb. 2, 1961, at the Conrad Hilton Hotel in Chicago, Illinois. The program will be open to members and nonmembers alike. The fee for the entire day, including lunch with the clinicians, is $25.00. Checks, made payable to the Association, should be forwarded to Dr. L. Parris, 1930 Chestnut St., Philadelphia, Pennsylvania. Attendance is limited.

Mid-Continent Dental Congress

The 1960 Mid-Continent Dental Congress, sponsored by the St. Louis Dental Society, will be held at the Chase Hotel in St. Louis, Missouri, Nov. 27 to 30, 1960. The schedule is as follows:

Sunday, November 27

Special four-hour course: "Practice Administration—Improve Dentistry Faster Without Increased Cost to the Patient." John L. Woehler, D.D.S., Sierra Madre, California.

Monday, November 28

Oral Rehabilitation. Ted Gordon, D.D.S., Chicago, Illinois.

Clinical Features and Recognition of Common Lesions of the Oral Mucosa. Lester W. Burket, D.D.S., M.D., Philadelphia, Pennsylvania.

Newer Concepts in Endodontics. George C. Stewart, D.D.S., Philadelphia, Pennsylvania.

Tuesday, November 29

Normal Functional Occlusion. Angelo D'Amico, D.D.S., Stockton, California.

Making Dentistry for Children Pleasurable and Profitable. Clinton C. Emmerson, D.D.S., Los Angeles, California.

What Place Has Periodontics in General Practice of Dentistry? Frank E. Beube, D.D.S., New York, New York.

Evaluation of Newer Dental Materials and Factors Affecting Their Clinical Success. Ralph W. Phillips, Indianapolis, Indiana.

Techniques for Positive Healing After Surgery. John C. Versnel, D.D.S., St. Louis, Missouri.

Wednesday, November 30

Complete Dentures. Vincent R. Trapozzano, D.D.S., St. Petersburg, Florida.

Additional information may be obtained from the St. Louis Dental Society, 8013 Maryland Ave., St. Louis 5, Missouri.

Southern California Academy of Endodontists

An all-day scientific meeting will be held at the Beverly Hills Hotel in Beverly Hills, California, on Saturday, Oct. 15, 1960, preceding the 1960 meeting of the American Dental

Association. The meeting will feature a nationally recognized guest speaker, table clinics, and a seminar luncheon. All members of the American Dental Association are invited to attend.

There will be a registration fee of $10.00 (including lunch). Checks should be mailed to Dr. Sanford Golden, Program Chairman, 1001 Gayley, Los Angeles 24, California.

Southern California Academy of Oral Pathology

The Academy will be host for a meeting on oral pathology at the Beverly Hilton Hotel in Los Angeles, California, on Oct. 16, 1960, the day preceding the opening of the American Dental Association meeting. Two outstanding oral pathologists—George Greene and Robert Gorlin—will be the featured essayists. All members of the American Academy of Oral Pathology and of organizations affiliated with ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY are cordially invited to attend.

Reservations and a check for $6.50 may be sent to the secretary, Dr. Arthur Barrett, 22030 Sherman Way, Canoga Park, California.

Sixteenth Australian Dental Congress

The Australian Dental Association will conduct the sixteenth Australian Dental Congress from Aug. 14 to Aug. 18, 1961, in Sydney, New South Wales. During the five-day scientific program there will be every opportunity to participate in a variety of lectures and clinics presented on all phases of dentistry and allied sciences. All dentists are cordially invited to attend the Congress.

Army Graduate School of Dentistry

The Army Graduate School of Dentistry, Walter Reed Army Institute of Research, Washington, D. C., announces the following postgraduate dental professional short courses:

Prosthodontics. Nov. 28 to Dec. 2, 1960.

Oral Surgery. Jan. 9 to 13, 1961.

Oral Diagnosis and Therapeutics. May 15 to 19, 1961.

Preventive Dentistry. June 5 to 9, 1961.

Attendance is open to (1) dental corps officers of the Armed Forces on active duty, (2) dental corps officers of the Armed Forces not on active duty, and (3) civilian dentists from other health agencies and communities near Walter Reed Army Institute of Research.

Boston University School of Medicine

The Department of Stomatology, Division of Graduate Studies, Boston University School of Medicine and the Massachusetts Memorial Hospitals, announces the following postgraduate courses:

Occlusal Adjustment. Bernard S. Chaikin, Henry M. Goldman, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. Sept. 12 to 16, 1960. $200.00.

Enodontics. Herbert Schilder. Sept. 12 to 16, 1960. $175.00.

Periodontal Therapy. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. Nov. 7 to 11, 1960. $175.00.

Fixed Bridge Prosthesis. Leo Talkov, David J. Baraban, and Lloyd Warshauer. Nov. 14 to 18, 1960. $175.00.

Full Denture Prosthesis. Chester Landy. Dec. 12 to 16, 1960. $150.00.

For further information about specific postgraduate courses and for application blank, write to Director of Postgraduate Courses, Department of Stomatology, Massachusetts Memorial Hospitals, 750 Harrison Ave., Boston 18, Massachusetts.

University of Mississippi

A conference on practice administration will be held Aug. 10 to 12, 1960. Two outstanding clinicians—F. Harold Wirth of New Orleans, Louisiana, and Harry M. Klenda of Wichita, Kansas—will participate.

Further information may be obtained from the Department of Conferences and Institutes, University, Mississippi.

Tufts University

Tufts University School of Dental Medicine will offer a special participation course in periodontology (DPG 605) Oct. 31 to Nov. 4, 1960. The course will be under the direction of Dr. Irving Glickman and staff. Tuition will be $175.00.

Emphasis will be placed on learning by clinical experience. The "bone factor" concept for the diagnosis, determination of prognosis, and treatment planning for individual teeth and for the dentition as a functioning unit will be explained in detail.

Further information may be obtained from the Director of the Division of Graduate and Postgraduate Studies, Tufts University School of Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Boston University Offers Course in Orthodontics

The Division of Graduate Studies of the Department of Stomatology announces that its graduate course in orthodontics will begin in September, 1960, under the direction of Dr. Herbert I. Margolis.

Further information may be obtained by writing to Boston University School of Medicine, Department of Stomatology, 80 East Concord St., Boston, Massachusetts.

REVIEWS OF THE LITERATURE

BOOK REVIEW

Xylocaine. Sten Wiedling. Stockholm, 1959, Almqvist and Wiksell (Astra Pharmaceutical Products, Inc., 7 Neposnet St., Worcester 6, Mass.).

This is an interesting survey of the clinical and pharmacologic actions of Xylocaine, based on a study of a large number of articles published on the subject. It deals with all aspects of the action of the drug—its local anesthetic action on peripheral nerves and on peripheral ganglia; its endoanesthetic actions; its action on the central nervous system, blood pressure, heart, blood, smooth muscle and striated muscle; and its allergic and toxic effects.

This is a monograph which should be read by all who use local anesthesia.

K. H. T.

ABSTRACTS OF CURRENT LITERATURE

Leukoplakia of the Bladder: A Precancerous Disease.
A. L. Shabad. Problems of Oncology **5**: 82, 1959.

Leukoplakia (literally, white plaques) is the term used to denote the areas of keratinizing, multilayer, squamous epithelium in the mucous membrane of the bladder. Thirty-two patients with leukoplakia of the urinary tract were seen in the urologic clinic of the First Moscow Medicinal Institute of the Order of Lenin in the last thirty-three years. There were nineteen men and twelve women, with an average age of 35 years.

Leukoplakia of the bladder develops in response to chronic inflammation and, unlike leukoplakic lesions of the oral cavity, does not tend toward malignant degeneration.

T. J. C.

The Problem of the Precancerous Lesion.
Fred W. Stewart. Postgrad. Med. **27**: 317, March, 1960.

The author, a well known pathologist, sets up certain principles regarding precancerous lesions. "The first principle is that the finding to your satisfaction that something is precancerous you haven't explained very much. You still do not know what caused the cancer. There is no direct uninterrupted line from normal to precancer to cancer. You still have to add something. A lesion is to be thought of as a precancerous if cancer is added more often to it though when it is not there."

"The second principle is that because a lesion looks quite like a malignant tumor, perhaps to such an extent that a pathologist not familiar with the process or who works without adequate clinical information will mistake it for cancer, it need not be either cancerous or precancerous."

Granular myoblastoma of the tongue is often confused with squamous carcinoma. This lesion looks like squamous cancer and is not precancerous. Tubercle and blastomycosis resemble carcinoma. A pathologist must have a knowledge of lesion behavior from personal experience and not merely know the histologic appearance of tissue and cells as a background for recognizing the precancerous state.

T. J. C.

Early Cancer of the Oral Cavity With Special Reference to Cancer of the Tongue.
A. J. Kremen and S. W. Arhelger. Postgrad. Med. 27: 421, March, 1960.

Lesions of the oral cavity are immediately available to inspection, palpation, and simple direct biopsy. The problem of precancerous lesions, carcinoma in situ, can be dealt with by local incision.

In diffuse carcinoma in situ, if invasive carcinoma is not found on biopsy, periodic examination and the elimination of irritants are recommended.

Treatment of cancer of the tongue is still a subject of controversy between surgeons and radiotherapists.

The authors used the technique of incontinuity resection of the tongue and floor of the mouth and neck dissection. The lesions were confined to one-half of the tongue or floor of the mouth, or both, and did not grossly extend beyond the midline. Operable cancer of the tongue, if treated aggressively by a complete cancer operation, will yield cure rates considerably in excess of those usually reported for this disease.

T. J. C.

Leukoplakia of the Intraoral Cavity.
William S. MacComb. Postgrad. Med. 27: 349, March, 1960.

In the oral cavity, leukoplakia has long been recognized as a precancerous condition. "Leukoplakia, meaning 'white plaque' is a lesion arising on mucous membranes of the external orifices of the human body."

Avitaminosis undoubtedly plays some part in the development of leukoplakia. For many years most authors have considered smoking in any form to cause the development of leukoplakia. It is felt that the end products of combustion are made up of various compounds, all of them highly irritating to the mucous membranes.

The use of alcohol has been suggested as a cause of intraoral leukoplakia. Usually, the buccal mucosa, gingiva, or gingivobuccal gutter is the area affected in the "snuff dipper."

There are three types of leukoplakia as it occurs in the oral cavity. The initial reaction to irritation is hyperemia; the second is elevated, thickened, and fissured but not ulcerated; and the third is ulcerated.

In the treatment, removal of the causal factors is the first step; cauterization and surgical excision are recommended for the latter stages.

T. J. C.

Intrathoracic Suppuration and Dental Sepsis.
R. H. Belsey. Brit. Dent. J. 107: 251, November, 1959.

The author, a thoracic surgeon, stresses the importance of having the mouth in hygienic condition before the induction of an inhalation anesthetic.

The inhalation of small particles of tartar may precipitate pulmonary infection. The inhaled tartar enters the small bronchiole and obstructs it. The segment of lung tissue supplied by this bronchiole becomes atalectatic and suppurative.

The use of an endotracheal tube may lead to contamination of the air passages.

Prophylaxis is the best management against infection in the lung. Oral sepsis, particularly periodontal disease, should be eliminated in patients selected for an elective surgical procedure.

T. J. C.

Oral Diagnosis of Systemic Disease.
E. S. Hopp. J. A. M. A. 168: 748, Oct. 11, 1958.

The author lists acute necrotizing stomatitis, erythema multiforme, lichen planus, aphthous stomatitis, and pemphigus as lesions of the oral mucosa associated with tension and nervous strain.

Tension, by affecting the autonomic nervous system, can alter circulation and reduce tissue resistance of the oral mucosa, which might promote bacterial and viral invasion. Careful examination and then explanation of the nature of the process constitute a necessary part of successful therapy. This can be supplemented in some instances by sedation, tranquilization, or mild local therapy.

T. J. C.

A Polyurethane Polymer (Ostamer): Its Use in Fractured and Diseased Bones. Report of Thirty-Five Cases.
M. P. Mandarino and J. E. Salvatore. A. M. A. Arch. Surg. 80: 623, April, 1960.

Thirty-five cases were treated with Ostamer* fixation for fractured and diseased bones. The results were gratifying.

Ostamer, a plastic which can be poured in liquid form, is reported to have properties of strength, osteogenesis, nontoxicity, and cohesiveness.

In addition to its use in fractures, it is recommended for use in bone cysts. New bone will grow through the plastic.

T. J. C.

Antibiotic-Induced Rectal Itch (Pruritus Ani) Treated With Amino-Acid Ointment.
T. M. Feinblatt and H. M. Feinblatt. Gastroenterology 38: 247, 1960.

A review of 427 cases of antibiotic-induced pruritus ani discloses that this condition is a common sequela of broad-spectrum antibiotics, especially chlortetracycline and oxytetracycline. The incidence of gastrointestinal side effects, including anal pruritus, has been estimated at 20 per cent of patients taking the recommended dosage of antibiotics. Without effective treatment, the symptoms are often severe and persistent. There appears to be no essential difference between idiopathic pruritus ani and the disease caused by antibiotics.

In a series of 100 cases of idiopathic pruritus ani and of 20 cases induced by antibiotics, the use of Hydrolamins amino-acid ointment provided immediate and permanent relief (88 per cent in the former group and 100 per cent in the latter). Results showed a superiority far better than anything expected in the treatment of pruritus ani. In the antibiotic group, the medication cleared up the rectal itch in a range of two to fourteen days (average, six days).

Hydrolamins amino-acid ointment contains 10 per cent lactalbumin hydrolysate, specially prepared to reduce the methionine and cystine content, in a polyethylene glycol base.

K. T.

*Ostamer is a trademark of the William S. Therrell Company, Cincinnati, Ohio, for its rigid polyurethane foam.